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THE RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN THE CARDIAC CYCLE OF MAN *

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In studying the dynamics of the heart beat, the relationship between electrical and mechanical events in the cardiac cycle has been of fundamental importance   The basic concepts of this relationship have been defined by Lewis (1925) and Wiggers (1923) and their co-workers   Sir Thomas Lewis provided indirect information on these events in the right auricle of man   Animal experiments, supplemented by such indirect information as could be obtained from venous and arterial pulse wave tracings, recording of heart sounds, etc , in man were used by Wiggers to anticipate the probable normal sequence of events in the cardiac cycle

More precise information may now be obtained using the method of right heart catheterization   With direct measurements from within the right heart chambers and pulmonary artery, coupled with peripheral arterial pulse wave and electrocardiographic recordings, the normal course of electrical and mechanical events may be more clearly defined in man and abnormalities in contraction and conduction of the diseased heart may be further elucidated

The data thus obtained will supplement the results obtained by many other investigators and will be analysed and discussed in the light of their studies

METHOD OF STUDY

In this study recordings of blood pressures in the auricle, ventricle, pulmonary artery, and brachial artery were made simultaneously with the electrocardiogram   The method of catheterization of the right heart, introduction of the indwelling arterial needle, and recording of pressures has been previously described (Cournand and Ranges, 1941, Cournand et al , 1944, and Bloomfield et al , 1946)   In some instances a double lumen catheter was used (Cournand et al , 1945), permitting the simultaneous recording of pressures in the right auricle and ventricle or the right ventricle and pulmonary artery   In order to obtain satisfactory records of these pressures, manometers of varying sensitivities were used   Only the records that permitted the exact determination of the onset of rise of pressure in the right heart or in the arteries were used   The electrocardiograph was of the string galvanometer type and tracings were usually made on standard lead II   The speed of the camera could be varied from 12 5 to 50 mm a second, permitting time intervals to be estimated correctly to within 0 010 sec   It has been shown repeatedly that no parallax exists between the light beams of the manometers and the electrocardiograph   A method for determining the time lag in mechanical transmission of an impulse through the catheter at 37° C has been previously described (Cournand et al , 1946), and on repeated determinations was found to be 0 010 sec   This applies to the initial pressure rise only   In analysing the records, a correction was therefore made by subtracting 0 010 sec from the measured values of the time intervals between the beginning of electrical and the beginning of mechanical events   In the present state of recording blood pressures in the right heart it is possible to determine exactly the point at which an initial pressure rise takes place   Because there is great uncertainty as to the accuracy of the records during the period of decline of pressure, analysis of the pressure curves during diastole was not attempted

B   1

The following measurements were made in analysing the records and the following symbols will be used in presenting the data

in man, " the upstroke of P precedes the upstroke of ' a ' in the human jugular curve by from 0 100 to 0 150 sec "

Beginning of the P wave of the electrocardiogram	P
Beginning of the Q wave of the electrocardiogram, or R, if Q is absent	Q
Beginning of auricular systole, marked by an ascension of the intra auricular pressure wave near the end of the diastolic period	At_s
Beginning of right ventricular systole, occurring at the end of diastole when the curve shows a steep rise	RV_s
Beginning of ejection in the pulmonary artery, marked by the rise of pressure in the artery, at the end of the descending diastolic curve	PA_s
Beginning of the systolic pressure rise in the brachial artery at the end of the descending diastolic curve	BA_s
Beginning of the systolic pressure rise in the femoral artery at the end of the descending diastolic curve	FA_s

The material for study was selected by analysis of all the records that had been obtained in the course of several years from normal subjects, children with congenital heart disease, and a variety of patients with cardiac or pulmonary disease

1 RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN ADULTS WITH ESSENTIALLY NORMAL CIRCULATION

In Table I will be found the average figures relating electrical and mechanical events in subjects with essentially normal circulation   Representative normal tracings are illustrated in Fig 1 and 3

(a) The average time interval between *the beginning of the P wave and the beginning of the auricular systole (P–At_s)* was 0 090 sec in 16 cases   This interval is somewhat less than that of 0 110 sec , found previously in 8 adult subjects with normal hearts by Cournand *et al* (1946)   Lewis (1925) has previously described the following relationship in dogs   " The upstroke of P precedes the curve of shortening in the right auricular appendage, in six dogs, by from 0 024 to 0 043 sec " The above values are about one third of what was found in normal adults in this study   Lewis also states that

In order to evaluate the pulse wave velocity in the large veins, tracings were taken in some of the present studies as the catheter was progressively withdrawn from the right auricle to the axillary region   Although such tracings are few, figures indicate that the pulse wave velocity in the undistended large veins of normal man progresses at approximately 2 5 metres a second   Assuming an average distance of 10 cm from the right auricle to the bulb of the right jugular vein, approximately 0 040 sec should be added to figures obtained by the catheterization technique in order to compare them with Lewis' figures in man

(b) The average time interval between *the beginning of Q and the beginning of the right ventricular systole (Q–RV_s)* was 0 075 sec in 30 cases   Lewis (1925) states that, " the beginning of the initial ventricular deflection usually precedes the onset of ventricular contraction, as estimated from myocardiograms from the front of the ventricle in six dogs, by from 0 020 to 0 038 of a second " Kahn *et al* (quoted by Wiggers, 1923), recording pressures by means of a needle in the right ventricle of dogs simultaneously with an electrocardiogram, found that the time interval from Q to the rise of pressure

TABLE I

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN ADULTS WITH ESSENTIALLY NORMAL CIRCULATION

Heart rate per minute	Average of 30 cases	80	—
P–R interval sec	Average of 30 cases	0 160	—
QRS interval, sec	Average of 30 cases	0 080	—
Q–BA_s interval, sec	Average of 30 cases	0 160	0 140–0 190
P–At_s interval, sec	Average of 16 cases	0 090	0·050–0 120
Q–RV_s interval, sec	Average of 30 cases	0 075	0 060–0 100
	Average of 15 cases*	0 072	—
Q–PA_s interval, sec.	Average of 15 cases*	0 085	0 070–0 100
End diastolic pressure in			
Right ventricle, mm Hg	Average of 15 cases*	3 0	—
Pulmonary artery, mm Hg	Average of 15 cases*	8 0	
Duration of isometric contraction of right ventricle, sec	Average of 15 cases*	0 013	0 010–0·020

* The same 15 cases were used to obtain these values

FIG 1 —Record illustrating normal electrical-mechanical time intervals in an adult subject
From top to bottom, blood pressure tracings in the brachial artery (B A) and the right atrium (R A) and electrocardiogram lead II
$P-At_s = 0.080$ sec $Q-BA_s = 0.160$ sec
In this and all other records the distance between vertical lines is equal to 0.040 sec
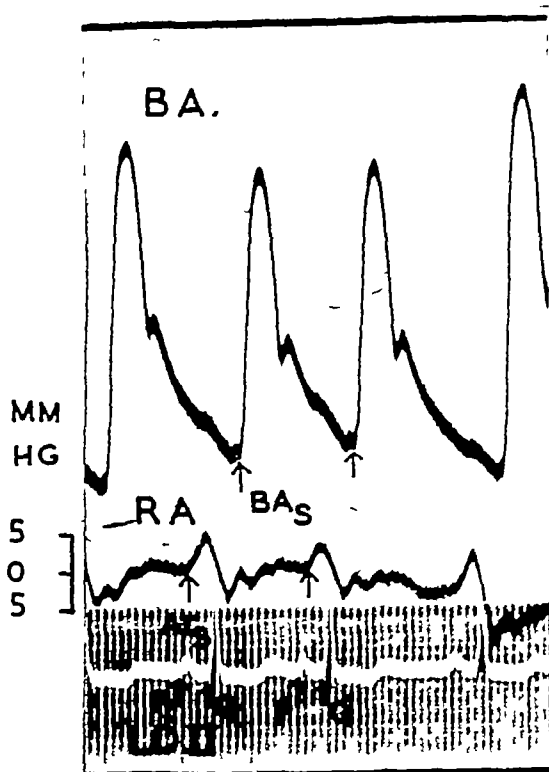
FIG 2.—Record illustrating electrical-mechanical events in a case with auricular premature contractions
From top to bottom, blood pressure tracings in the brachial artery (B A), the right atrium (R.A), and electrocardiogram lead II   P' and Q' correspond to the premature beat

was from 0.031 to 0.035 sec   Garten (quoted by Wiggers, 1923), using an electrical manometer, found approximately the same interval—0.030 to 0.045 sec An analysis of a tracing of Wiggers (1928) shows the same interval to be 0.040 sec   These figures in dogs are about one half of the values found in man in the present study   In an analysis of the time interval between the beginning of the electrical ventricular complex and the c wave in jugular tracings of man, Lewis states that   the upstroke of R precedes the upstroke of c in the human jugular by from 0.100 to 0.150 of a second '   Miller and White (1941) found an identical value for the Q–c interval in man Assuming that the c wave corresponds to the beginning of the mechanical contraction in the right ventricle and subtracting 0.040 sec for its transmission to the jugular, the figures compare well with the Q–RVₛ time as measured directly

(c) The average time interval between *the begin-*

ning of Q and the beginning of the pulmonary artery systole $(Q-PA_s)$ was 0.085 sec   Using this time interval, it is possible to measure the duration of the isometric contraction of the right ventricle, i e the time required to raise the pressure from the end diastolic level in the right ventricle to the end diastolic level in the pulmonary artery   This time is calculated by subtracting the value of $Q-RV_s$ from $Q-PA_s$ In 15 cases where both right ventricle and pulmonary artery pressures have been measured, the value for this interval was 0.013 sec   A tracing of simultaneous pulmonary artery and right ventricular pressures, taken with a double lumen catheter (Fig 3), demonstrates the short duration (0.010 sec) of the isometric contraction in a normal subject   In the 15 cases studied, the average pressure values were, respectively, 3 mm Hg for the end diastolic pressure in the ventricle and 8 mm Hg for the end diastolic pressure in the pulmonary artery   A period
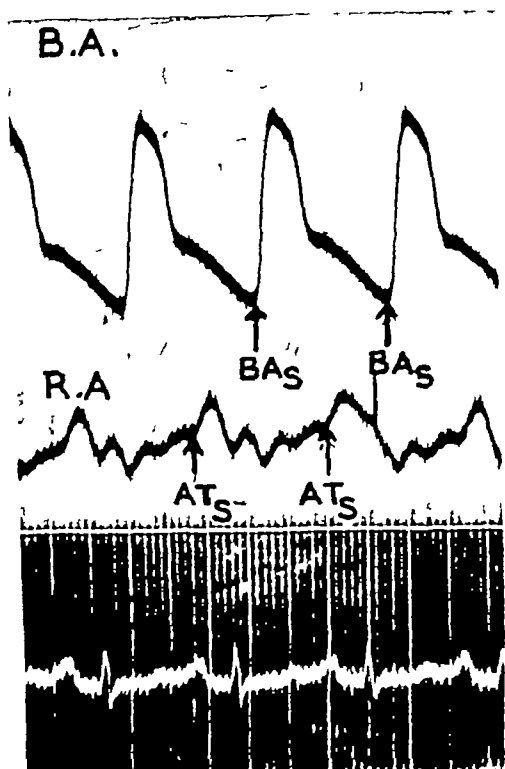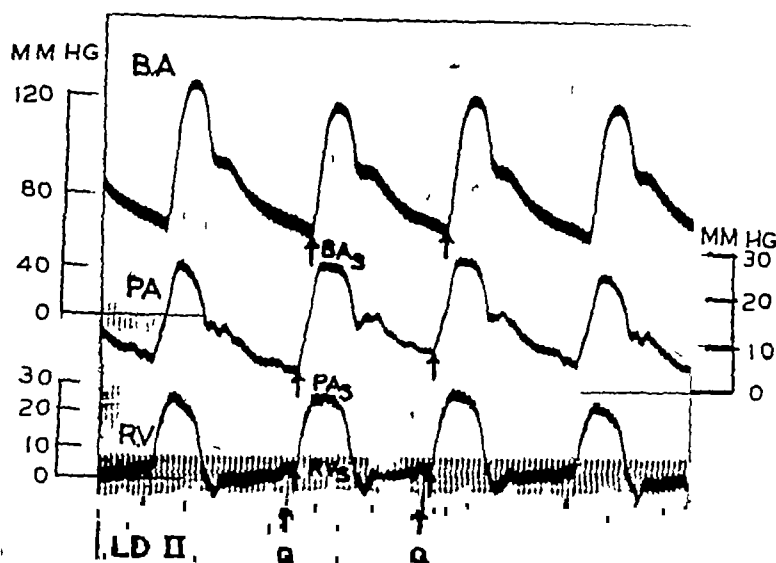
FIG 3 —Record illustrating normal electrical mechanical time intervals in an adult subject
    From top to bottom, blood pressure tracings in the brachial artery (B A), the pulmonary artery (P A), the right ventricle (R V), and the electrocardiogram lead II   The intracardiac blood pressure tracings were taken simultaneously with a double lumen catheter
    Note that the slope of the ascending pressure curves in the right ventricle and pulmonary artery do not exactly coincide   This may represent a genuine difference or be a manifestation of hysteresis in the recording   Regardless of the interpretation given to this difference, it has no bearing upon the choice of the exact site of the initial rise in pressure
Q–RV$_s$ = 0 080 sec   Q–PA$_s$ = 0 090 sec   Q–BA$_s$ = 0 160 sec
    The duration of isometric contraction is 0 010 sec

of 0 013 sec was therefore necessary to raise the pressure in the right ventricle 5 mm Hg above the initial level in order to open the pulmonary valves

(d) The average time interval between *the begin-ning of Q and the beginning of brachial artery systole* (Q–BA$_s$) was found to be 0 160 sec in 30 cases   Assuming that the pulse wave velocity does not vary greatly, this time interval is probably valuable in assessing indirectly the duration of isometric con-traction of the left ventricle   By simultaneous registration of heart sounds, subclavian pulse, and the electrocardiogram in man, Wiggers (1944) estimated the duration of isometric contraction in the left ventricle to be from 0 040 to 0 060 sec   Katz and Feil (1923) found figures with a somewhat greater range, 0 024 to 0 089 sec   With an average duration of isometric contraction of the left ven-tricle of 0·050 sec , 0 110 sec would be required for the pulse wave to be transmitted to the brachial artery   This corresponds approximately to a pulse wave velocity of 5 metres a second   Previously published values for the time interval between the

beginning of Q and the onset of pressure rise in the more proximal arteries will be found in Table II

2   RELATIONSHIP BETWEEN ELECTRICAL AND MECHA-
    NICAL EVENTS IN CHILDREN WITH CONGENITAL
    HEART DISEASE

In Table III will be found the average figures in children whose ages range from 5 months to 16 years   On the whole, the intervals were shorter than in normal adults

(a) *The average P–AT$_s$ time interval* was 0 060 sec in 16 cases   In a previously reported case of a child 8 years of age with tetralogy of Fallot, a value of 0 055 sec was found, Cournand et al , 1946   The question arose as to whether the P–AT$_s$ time varies with the age of the subjects   In general it was found that the younger the child the shorter the P–AT$_s$ time although the correlation did not appear to be extremely close   In Fig 4 is illustrated the P–AT$_s$ time interval in a child of 3   In general, the nature of the congenital disease did not appear to exert a great influence on this time interval   In two

TABLE II

PREVIOUSLY PUBLISHED VALUES FOR THE TIME INTERVAL BETWEEN THE BEGINNING OF Q AND THE ONSET OF ARTERIAL PRESSURE RISE (IN SECONDS)

Author	Interval studied	Range	Average
Nichol (1933)	Q to rise of pressure in subclavian artery	0 119–0 166	0 135
Wolferth *et al* (1935)	Q to rise of pressure in carotid artery	0 090–0 150	0 111
Katz *et al* (1935)	Q to rise of pressure in subclavian artery	0 100–0 160	0 120
Battro *et al* (1936)	Q to rise of pressure in carotid artery	0 060–0 120	—
Castex *et al* (1941)	Q to rise of pressure in carotid artery	0 080–0 160	0 120
Kossmann *et al* (1947)	Q to rise of pressure in carotid artery	0 131–0 148	0 139
Present study (1948)	Q to rise of pressure in brachial artery	0 140–0 190	0 160

TABLE III

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN CHILDREN WITH CONGENITAL HEART DISEASE

Heart rate per minute	Average of 23 cases	109	—
PR interval, sec	Average of 23 cases	0 140	—
QRS interval, sec	Average of 23 cases	0·060	—
Q–BA$_s$ interval, sec	Average of 23 cases	0 150	0 140–0 190
P–At$_s$ interval, sec	Average of 16 cases	0 060	0 030–0 090
Q–RV$_s$ interval, sec	Average of 23 cases	0 058	0 040–0 100
	Average of 12 cases*	0 056	
Q–PA$_s$ interval, sec	Average of 12 cases*	0 079	0 050–0 110
End diastolic pressure in			
Right ventricle, mm Hg	Average of 12 cases*	5 0	—
Pulmonary artery, mm Hg		18 0	
Duration of isometric contraction of right ventricle, sec	Average of 12 cases*	0 023	0 010–0 030

* The same 12 cases were used to obtain these values
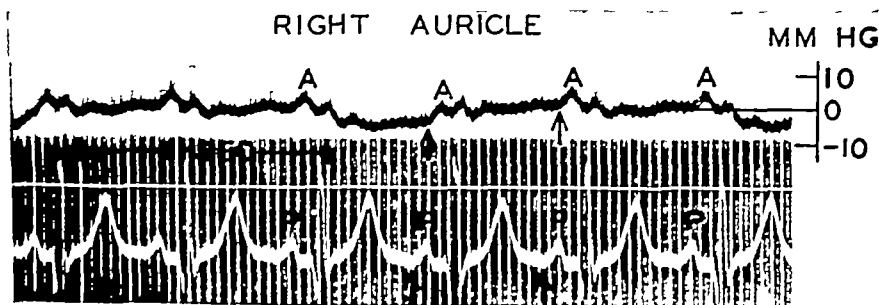
FIG 4 —Record illustrating electrical mechanical time intervals in a child of 3 years with congenital heart disease

From top to bottom, blood pressure tracings in the right atrium and electro-cardiogram lead II The electrocardiographic standardization is 1 millivolt = 2 centimetres

cases of interauricular septal defect the P–AT$_s$ times in the right and in the left auricles were identical, i e 0 060 sec

(*b*) *The average Q–RV$_s$ time interval,* extending from the initial deflection of the QRS complex to the beginning of the right ventricular systole was 0 058 sec in 23 cases No significant relationship could be found between this time interval and the nature of the defect or the age of the subject It is, however, important to note that in all types of congenital defects, even in the cases with hypertrophy and dilatation of the right ventricle, the duration of Q–RV$_s$ was never greater than in normal adults In one case of interventricular septal defect the

Q–V$_s$ time intervals were the same in the right and in the left ventricle, i e 0 070 sec (Fig 5)

For lack of knowledge of the exact onset of the initial electrical deflection corresponding to activation in each of the four separate chambers of the heart, no conclusion can be drawn from the figures given in this and the previous section as to the spread of excitation and beginning of contraction in each chamber

(c) *The average Q–PA$_s$ time interval* was 0 079 sec in 12 cases   The difference between this figure and the Q–RV$_s$ time interval in these 12 cases, represented an average duration of isometric contraction in the right ventricle of 0 023 sec , with a range of 0 010 to 0 030 sec   Since the average pressure values at the end of diastole in the right ventricle and in the pulmonary artery were 5 mm Hg and 18 mm Hg respectively, this time interval (0 023 sec) was required to raise the pressure in the right ventricle by 13 mm Hg   This increase in the duration of isometric contraction was therefore due to hypertension in the lesser circulation   In a case of patent ductus arteriosus studied before and after ligation a change in the duration of isometric

contraction was noted   As seen in Table IV, 0·030 sec was required to raise the pressure in the right ventricle 36 mm Hg   before operation   After ligation the duration of isometric contraction was reduced to 0 010 sec for a pressure rise in the right ventricle from 1 to 5 mm Hg

(d) *The average Q–BA$_s$ time* was 0 150 sec in 23 cases   This figure is almost identical with that found in adults, although the distance between the heart and the peripheral artery is obviously less   If one assumes that the time of isometric contraction in the left ventricle is approximately the same in children as in adults, then the pulse wave velocity must be much slower in children   This finding is not unexpected because of the greater deformability of the arterial walls in young subjects

3 RELATIONSHIP BETWEEN ELECTRICAL AND MECHA NICAL EVENTS IN ADULT PATIENTS WITH CARDIO- VASCULAR DISEASE

(a) *Normal Sinus Rhythm with no Conduction Abnormalities*

In Table V will be found the average figures relating electrical and mechanical events in a group
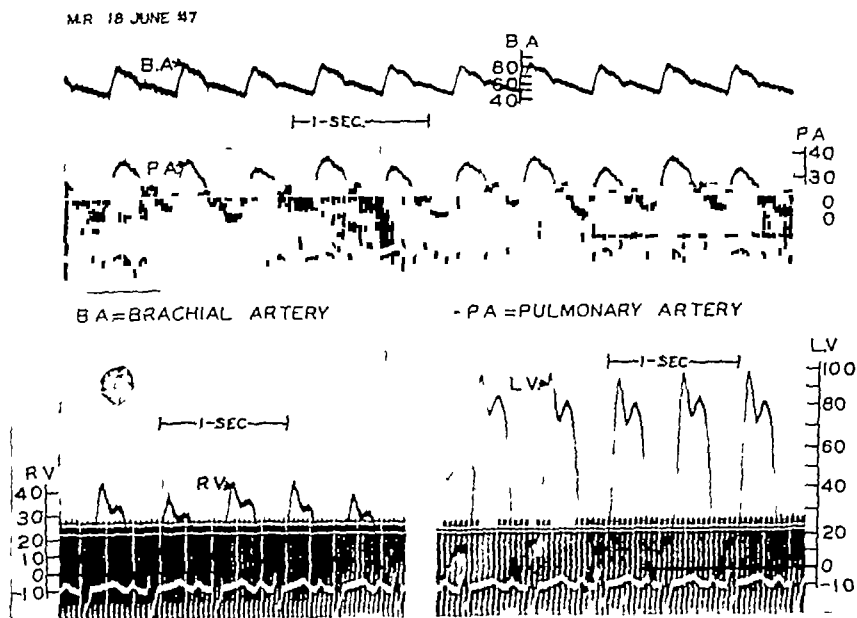
FIG 5 —Records illustrating electrical mechanical events in a case with interventricular septal defect
   Upper row from top to bottom blood pressure tracings in the brachial artery (B A) and the pulmonary artery (P A)   Lower row at left, blood pressure tracing in the right ventricle (R V), at right, blood pressure tracing in the left ventricle (L V)
   Note that the tracings in the ventricles may show some evidence of overshooting
   Q–RV$_s$ = 0 070 sec   Q–PA$_s$ = 0 080 sec   Q–LV$_s$ = 0 070 sec   Q–BA$_s$ = 0 150 sec
                  R V = Right ventricle   L V = Left ventricle
   All pressures in mm Hg   Electrocardiogram, lead II

TABLE IV

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS BEFORE AND AFTER LIGATION IN A CASE OF PATENT DUCTUS ARTERIOSUS

	Before ligation	After ligation
Q–RV$_s$ interval, sec	0 060	0 050
Q–PA$_s$ interval, sec	0 090	0 060
Duration of isometric contraction of right ventricle, sec	0 030	0 010
End diastolic pressure in		
Right ventricle, mm Hg	0	1 0
Pulmonary artery, mm Hg	36 0	5 0

TABLE V

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN ADULTS WITH CARDIOVASCULAR DISEASE

Heart rate per minute	Average of 21 cases	85	—
PR interval, sec	Average of 21 cases	0 180	—
QRS interval, sec	Average of 21 cases	0 080	—
Q–BA$_s$ interval, sec	Average of 21 cases	0 170	0 140–0 210
P–At$_s$ interval, sec	Average of 21 cases	0 083	0 050–0 100
With normal right heart pressures			
Q–RV$_s$ interval, sec	Average of 8 cases	0 074	0 070–0 090
Q–PA$_s$ interval, sec	Average of 8 cases	0·088	0 080–0 110
End diastolic pressure in			
Right ventricle, mm Hg	Average of 8 cases	3 0	—
Pulmonary artery, mm Hg	Average of 8 cases	7 0	—
Duration of isometric contraction of right ventricle, sec	Average of 8 cases	0·014	0 010–0 020
With elevated right heart pressures			
Q–RV$_s$ interval, sec	Average of 13 cases	0 073	0 060–0 090
Q–PA$_s$ interval, sec	Average of 13 cases	0 096	0 080–0 120
End diastolic pressure in			
Right ventricle, mm Hg	Average of 13 cases	7 0	—
Pulmonary artery, mm Hg	Average of 13 cases	32 0	—
Duration of isometric contraction of right ventricle sec	Average of 13 cases	0 023	0 010–0 050

of 21 patients with various types of cardiovascular disease including congenital, rheumatic, hypertensive, arteriosclerotic, and cor pulmonale

In all these patients the P–At$_s$, Q–RV$_s$, and Q–BA$_s$ time intervals were approximately the same as in normal adults regardless of the presence or absence of cardiac failure

The Q–PA$_s$ time interval studied in 8 cases of heart disease with normal right heart and pulmonary artery pressures (without evidence of congestive failure) was identical with the figure found in normal adults In 13 patients with elevated right heart and pulmonary artery pressures and evidence of congestive failure, the average Q–PA$_s$ time interval was slightly prolonged although the range did not differ greatly from the normals

The average duration of the isometric contraction of the right ventricle in cardiacs with normal right heart pressures was 0 014 sec, essentially a normal figure This interval was required to raise the pres-

sure in the right ventricle from an average of 3 to 7 mm Hg In the patients with congestive failure an average of 0 023 sec was required to raise the pressure from 7 to 32 mm Hg a difference of 25 mm This figure falls within the normal variation but the range was greater, and in some cases with hypertension of the lesser circulation, isometric contraction was markedly prolonged As can be seen in Fig 10 (see p 12), there appears to be a trend of correlation between the duration of isometric contraction of the right ventricle and the magnitude of the pressure difference between the end diastolic levels of the right ventricle and the pulmonary artery

(b) *Abnormalities of Rhythm, Conduction, and Contraction* (1) *Auricular premature contractions*

Auricular premature beats were observed in three patients In two, pressures were recorded in the right auricle, and in the third in the right auricle and right ventricle A representative tracing is seen in

Fig 2 (see p 3)   There was no demonstrable difference in the P-At$_s$, Q-RV$_s$, and Q-BA$_s$ time intervals in the premature beat as compared to the sinus beat   It should be noted that in all these cases the degree of prematurity was not marked

(2) *Ventricular premature contractions*

The data that form the basis of this analysis were accumulated at random   It is therefore obvious that a systematic study, using more complete electro-cardiographic data (conventional and endocardial leads), is required to confirm and amplify the findings reported here   In particular the problem of induced right ventricular premature contractions should be greatly clarified by a well planned study

In this report emphasis will be placed only upon the following points   (a) asynchronism of the two ventricles, (b) nature and character of auricular events during the premature ventricular contractions, (c) relationship between premature contraction and arterial systolic rise

(a) *Ventricular asynchronism and its relationship to the site of origin of the premature ventricular contractions*   The type of ventricular asynchronism produced by premature ventricular contractions can be identified by examination of mechanical events recorded simultaneously on both sides of the heart. A prolongation of the Q-RV$_s$ time alone suggests a delay in contraction of the right ventricle, while prolongation of the Q-BA$_s$ time points to a delay in left ventricular contraction

However, in order to compare the Q-BA$_s$ time interval of the normal beat and the premature contraction, it was necessary to read the Q-BA$_s$ times at the same pressure levels   Since the diastolic
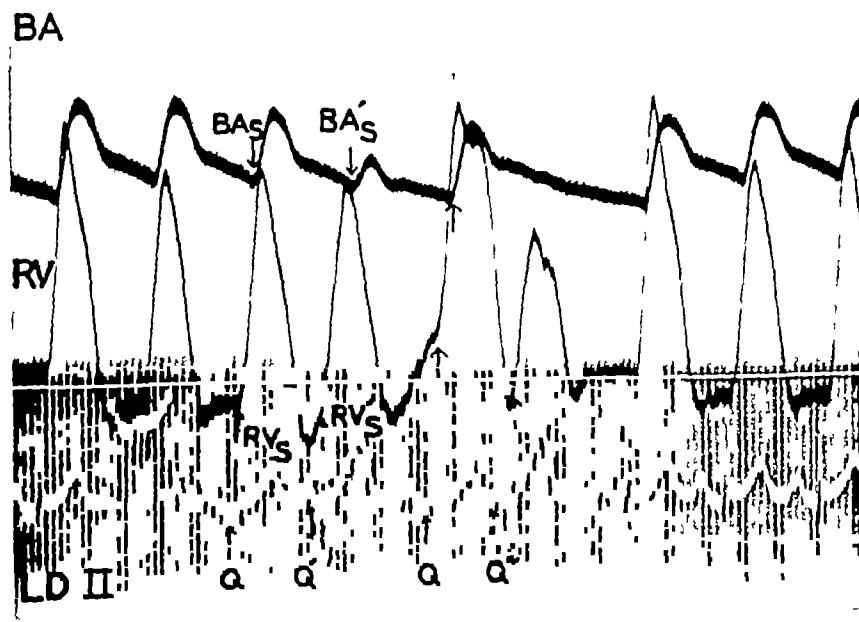
FIG 6 —Record illustrating electrical-mechanical events in a case with ventricular premature contractions
From top to bottom, blood pressure tracings in the brachial artery (B A) the right ventricle (R V), and electrocardiogram lead II   Q and Q correspond to premature contractions
Q-BA$_s$ = 0 130 sec   Q-RV$_s$ = 0 060 sec   Q -BA$_s$ = 0 210 sec   Q -RV$_s$ = 0 060 sec
Q-Q = 0 44 sec   Q-Q = 0 38 sec
Note that Q   is not followed by demonstrable pulse wave in the brachial artery and corresponds to a low pressure rise in the right ventricle

pressure in the aorta will be higher the earlier the premature contraction, it was arbitrarily decided to read the Q–BA$_s$ time for the normal beat at the initial pressure level of the premature beat

The majority of ventricular premature beats studied, showed as the striking characteristic, a lengthening of the Q–BA$_s$ time (average of 9 cases, 0 227 sec , range 0 180 to 0 270 sec) while the Q–RV$_s$ time remained normal (average of 9 cases, 0 074 sec , range 0 060 to 0 100 sec)   An illustrative example is shown in Fig 6

However, in one patient in whom numerous premature beats were observed, the Q–BA$_s$ time intervals in the sinus and premature beats were respectively 0 140 and 0 150 sec   In contrast, the Q–RV$_s$ time of the sinus beats varied from 0 060 to 0 070 sec while the Q–RV$_s$ times of the premature beats were 0·070 to 0 100 sec

In summary, the ventricular asynchronism found suggests that there was a delay in left ventricular contraction in the first group of 9 patients, whereas in one case the observations point to a delay in right ventricular contraction   Whether the delay was due to abnormalities of contraction or spread of excitation or both, is a matter of conjecture

The relationship between the type of ventricular asynchronism and the site of origin of the ventricular premature beats is of considerable interest   In the first group of 9 patients the site of origin of most of these spontaneous premature contractions could not be identified since the majority of pressure recordings

were made simultaneously with lead II of the electrocardiograph   However, the type of ventricular asynchronism suggests a right ventricular origin for these beats

In the single patient previously discussed, the type of ventricular asynchronism suggests a left ventricular origin for all the premature beats   However, the successive premature contractions as recorded on lead I were of such different electrical configurations as to suggest both right and left ventricular origins   In addition, in a second case a similar situation was found   In this instance two isolated premature beats with QRS deflections in opposite directions were recorded in lead I (Fig 7)   It is seen that while the normal beat shows a Q–RV$_s$ time interval of 0 070 sec the same interval measures 0 170 sec in the first premature beat and 0 150 sec in the second   There was no pressure wave in the brachial artery tracing corresponding to the ectopic beats, indicating absence of ejection into the aorta and, therefore, no information as to the events in the left ventricle could be obtained

It is obvious from the two cases just cited that it is difficult to interpret the relationship between electrical configuration of the premature contractions and the mechanical events, since different electrical patterns gave the same type of ventricular asynchronism

In the only investigations so far reported in man relating to this type of asynchronism, Castex, Battro, and Gonzales (1941) have shown that in premature
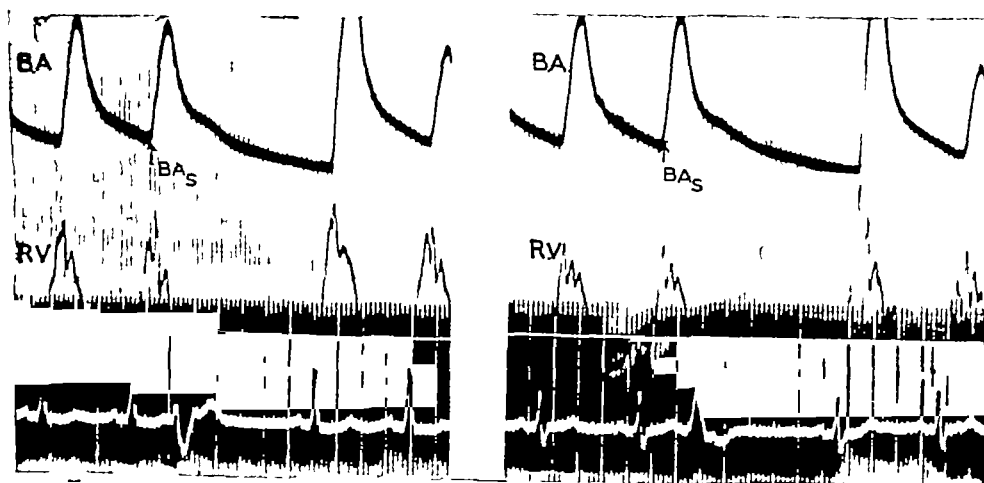
FIG 7 —Records illustrating electrical mechanical events in a case with ventricular premature contractions characterized by different electrical patterns
From top to bottom, blood pressure tracings in the brachial artery (B A), the right ventricle (R V) and electrocardiogram lead I
In the electrocardiogram to the right an S wave has appeared indicating right bundle branch block induced by quinidine   Ventricular tracings show many artifacts but the early systolic pressure rise can be defined

beats there is a very significant increase in the time interval between the onset of the QRS complex and the beginning of pressure rise in the subclavian artery. In 76 normal subjects the time interval averaged 0 120 sec, while in 10 cases of right ventricular premature contractions, it averaged 0 220 sec. An unexpected finding was the prolongation of the time interval between Q and the pressure rise in the subclavian artery in 13 cases of left ventricular premature contractions

(b) *Nature and character of auricular events during the premature ventricular contractions*   In 6 cases of ventricular premature beats, tracings of right auricular pressure waves showed a rise in pressure, A', occurring during and immediately following ectopic ventricular complexes. This is in contrast to the usual drop in pressure accompanying the descent of the base at the onset of ventricular systole. Examples of such tracings are seen in Fig 8 and 9. The question arises as to whether these pressure waves, A', were related to tricuspid insufficiency, bulging of the valve during ventricular isometric contraction, or to auricular systole of sinus or retrograde origin. In some instances a P wave could be detected in the S–T segment of the premature beats. These P waves preceded by the usual P-AT$_s$ time interval, the auricular pressure rise, A'. In other instances no auricular deflection could be identified within the QRS complex or S–T segment. In both instances the time interval separating the previous auricular systole and A' was identical with the distance

between the normal auricular systoles regardless of the time at which the ventricular premature contraction appeared. This indicates that A' in these instances is the result of a normal auricular systole

These findings are in agreement with observations of Lewis (1925) on premature beats as illustrated in his monograph (Fig 182, page 212). In summary, it can be assumed that even when a premature ventricular beat occurs, the spread of stimulation from the sinus node may take place undisturbed and initiate a normal auricular contraction

(c) *Relationship between ventricular ejection and degree of prematurity*   It is a clinically established fact that some premature beats are followed by ejection of blood into the aorta, while some are not. With simultaneous recordings of the electrocardiogram and pulse waves in brachial artery and pulmonary artery, it is possible to obtain information concerning the shortest time interval between a normal sinus and a premature beat (Q–Q interval) that gives rise to ejection of blood from the right and left ventricles, and the relation between this time interval and the heart rate. Table VI and Fig 11 give data obtained in 9 patients concerning these problems. All the tracings showed several premature contractions occurring at various intervals after the sinus beats. In three of these cases pulmonary artery tracings were also available. It is seen that the shortest time interval between a sinus beat and a premature beat followed by left or right ventricular ejection varied with the rate and ranged between
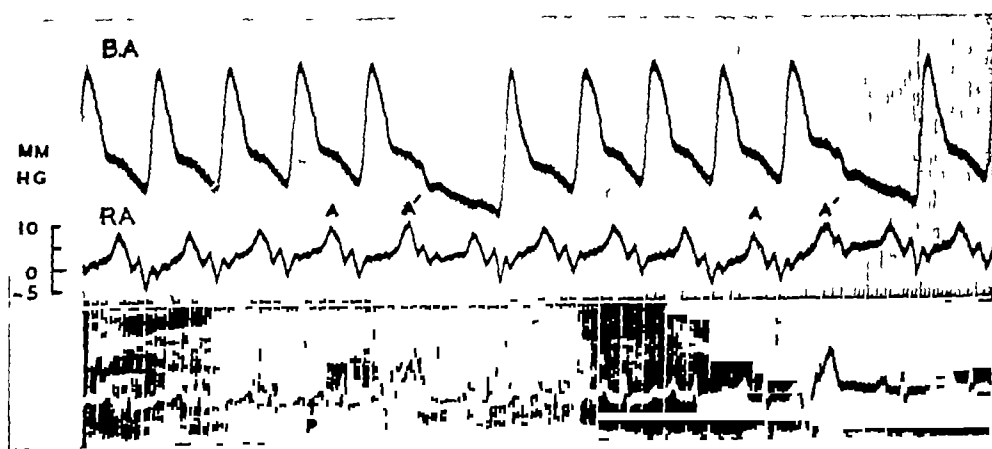

FIG 8 —Record illustrating electrical mechanical events in the atrium in a case with ventricular premature contractions

From top to bottom blood pressure tracings in the brachial artery (B A), right atrium (R A) and electrocardiogram lead II

Note that the interval A–A is equal to the normal auricular cycle time indicating that the sinus rhythm is undisturbed by premature contractions
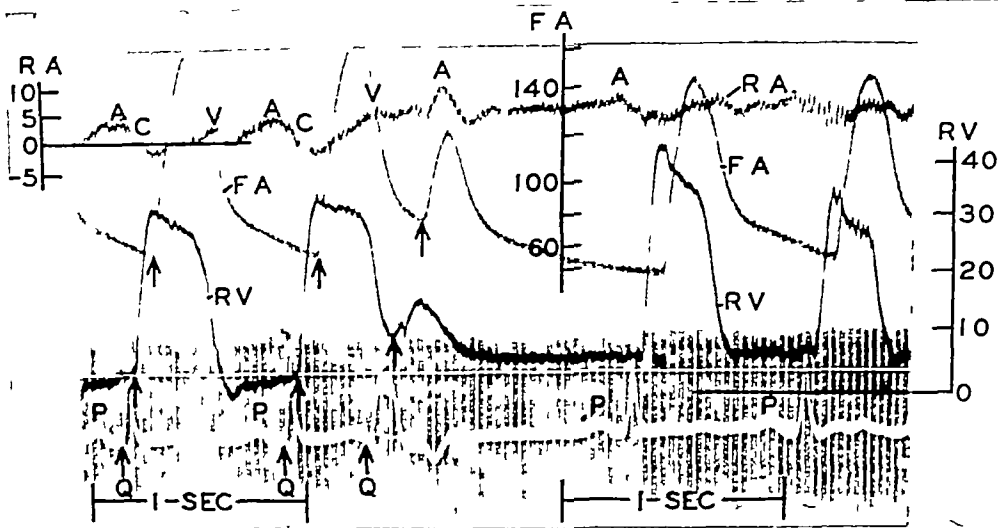
FIG 9—Record illustrating electrical-mechanical events in a case with ventricular premature contractions

From top to bottom, blood pressure tracings from the right atrium (R.A), the femoral artery (F A), the right ventricle (R V), and electrocardiogram lead II   For discussion see text   The blood pressure tracings in the right atrium and right ventricle were taken with a double lumen catheter

Note that the brachial artery tracing shows left ventricular output following the premature contraction and that the corresponding right ventricular pressure curve starts during isometric relaxation   This is strong evidence in favour of the presence of residual blood at the time of the premature contraction

F A = Femoral artery   R V = Right ventricle   R A = Right auricle   Electrocardiogram, lead II   A–C–V waves marked on R Aur   All pressures in mm Hg

TABLE VI

RELATIONSHIP BETWEEN HEART RATE AND THE MINIMUM EJECTION TIME IN THE BRACHIAL AND PULMONARY ARTERIES IN NINE CASES WITH VENTRICULAR PREMATURE BEATS

Case no	Duration of the normal cycle sec	Heart rate per minute	Shortest Q–Q * interval followed by ejection in the	
			Brachial artery, sec	Pulmonary artery sec
317	0 460	130	0 340	0 340
315	0 540	111	0 400	—
348	0 680	88	0 440	0 440
345	0 720	83	0 410	—
316	0 760	79	0 510	0 480
350	0 780	78	0 480	—
306	0 780	78	0 450	—
313	0 920	65	0 500	—
320	1 040	58	0 640	—

* Q–Q interval is the time interval between the beginning of the QRS of the sinus beat and the beginning of the QRS of the ventricular premature beat

0 340 sec at 130 beats a minute and 0 640 sec at 58 beats a minute   The remarkable straight line relationship of all intermediate points is well illustrated in the graph (Fig 11)

In summary at a rapid rate an early premature beat was followed by ejection of blood into the aorta and pulmonary artery, whereas, at a slower rate, a ventricular contraction with the same degree of prematurity did not produce a pressure rise in the arterial tracings   These observations can best be explained by the more rapid early diastolic filling of the heart at faster rates
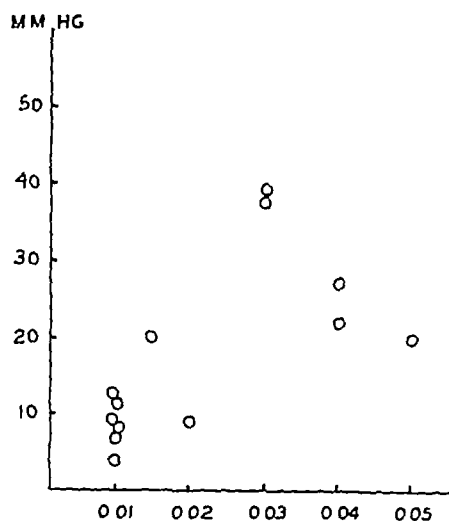
FIG 10 —Correlation between the duration of isometric contraction and the corresponding pressure rise in the right ventricle in thirteen subjects including normal cases and cases with cardiac failure *The vertical scale shows the end diastolic pressure difference between the right ventricle and the pulmonary artery The horizontal scale shows the isometric contraction time in seconds For discussion see text*
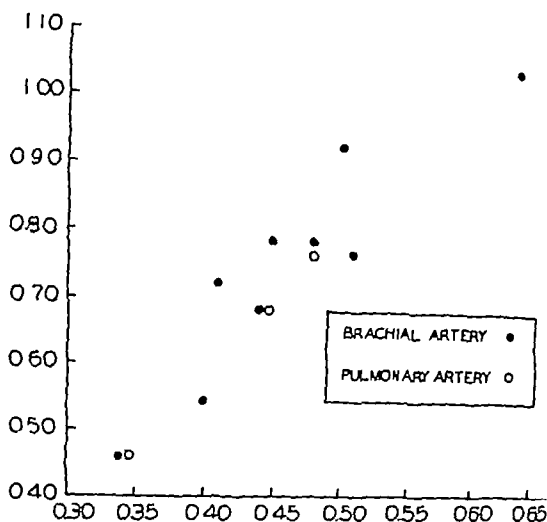

FIG 11 —Correlation between heart rate and the shortest time interval between a normal beat and a premature contraction resulting in ejection of blood into the aorta or pulmonary artery *The horizontal scale shows the Q–Q interval in seconds the vertical scale shows the duration of the normal cycle in seconds*

(3) *Auricular Fibrillation*

A study of the relationship between cycle length and Q–RV$_s$ and Q–BA$_s$ time intervals was made in three cases of arteriosclerotic heart disease with chronic auricular fibrillation *Significant variations as large as 0 070 sec were found in the Q–RV$_s$ and Q–BA$_s$ intervals of successive beats, although the QRS complexes had essentially the same configuration and duration No constant relationship was found between cycle length and these variations in the electrical-mechanical time intervals In addition, the Q–RV$_s$ and Q–BA$_s$ intervals of the same beat did not vary to the same degree, as illustrated in Fig 12 These findings suggest that, besides the complete arrhythmia, disturbances of the contraction mechanism of both ventricles were present*

(4) *Auricular Flutter*

Two cases of auricular flutter were studied In one of the cases observations were made on the P–AT$_s$ time during a period with pure flutter and a 4 1 A-V response *The electrocardiogram and right auricular tracings are shown in Fig 13 and demonstrate the regular sequence of electrical and mechanical events The duration of the P–AT$_s$ time of each auricular systole was 0 070 sec , a figure slightly lower than the normal mean, but within the*

normal range of variation *In this and a second case, varying degrees of block were also observed Pressure tracings in the right auricle, right ventricle, and brachial artery were recorded and are illustrated in Fig 14 It is seen that the 3 1 cycle with its longer ventricular diastolic filling period was followed by a larger pressure rise in the brachial artery and right ventricle than was the 2 1 cycle with its shorter filling period The auricular pressure tracings were not influenced by the degree of block, while the brachial artery and right ventricular pressures were dependent on the time at w | t the QRS fell in relation to isometric relaxatio ʼn addition, it was found that the Q–BA$_s$ time o ˘ak beat was longer by 0 020 sec than the ˎ ₅ time of the strong beat, if both beats were read at the same pressure levels This suggests that the duration of isometric contraction was prolonged following poor filling of the ventricles Similar observations regarding the influence of the varying A-V response upon the brachial artery pressure are seen in Fig 15 which illustrates a case of auricular flutter with successive 3 1, 2 1, 1 1 A-V ratio*

(5) *Heart Block*

Nine cases with different types of heart block were studied, two cases of complete heart block with idio-
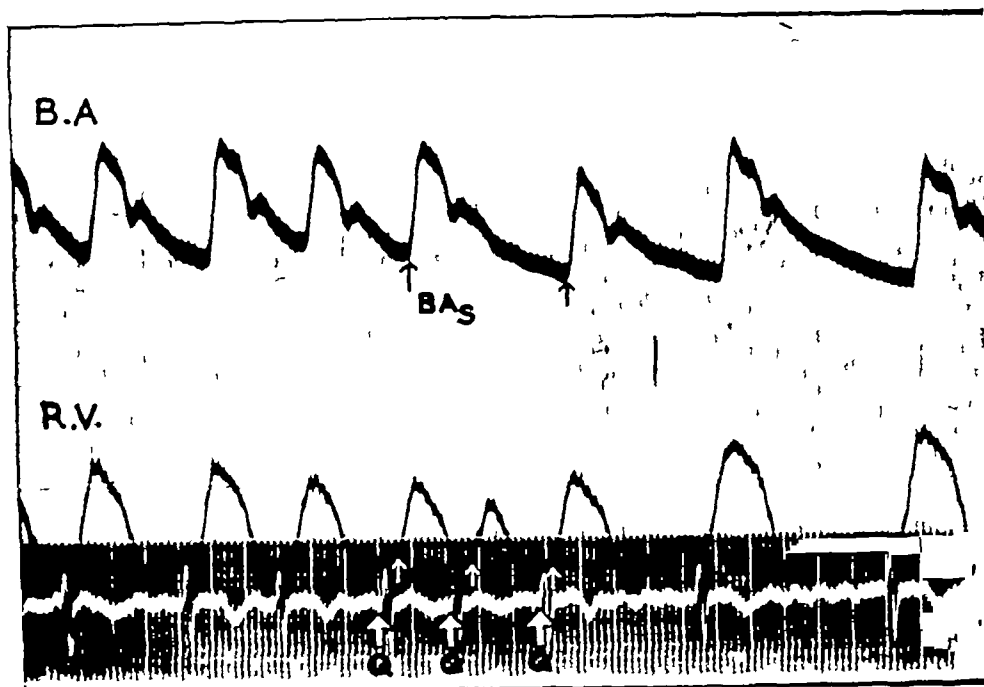
FIG 12 —Record illustrating electrical mechanical events in a case of auricular fibrillation
From top to bottom, blood pressure tracings in the brachial artery (B A), right ventricle (R V), and electrocardiogram lead II
In the three beats indicated by arrows the successive Q–RV$_s$ and Q–BA$_s$ times were first beat, Q–RV$_s$ = 0 110 sec and Q–BA$_s$ = 0 190 sec , second beat, Q–RV$_s$ = 0 110 sec and Q–BA$_s$ not measurable third beat, Q–RV$_s$ = 0 070 sec and Q–BA$_s$ = 0 170 sec

FIG 13 —Auricular flutter Record illustrating electrical mechanical events in a case with a 4 1 A V response
From top to bottom, right atrial blood pressure tracings and electrocardiogram lead II For discussion see text

ventricular rhythm originating in the His bundle, one case of incomplete A-V heart block, two cases of left bundle branch block, two cases of right bundle branch block, and two cases of right bundle branch block with 2 1 A-V heart block, one of which showed runs of complete heart block

(a) *Complete heart block* The two cases with complete heart block had P waves and QRS complexes of normal duration The data relating to the duration of the time intervals between electrical and mechanical events will be found in Table VII As was to be expected, the P–AT$_s$, the Q–RV$_s$, and the
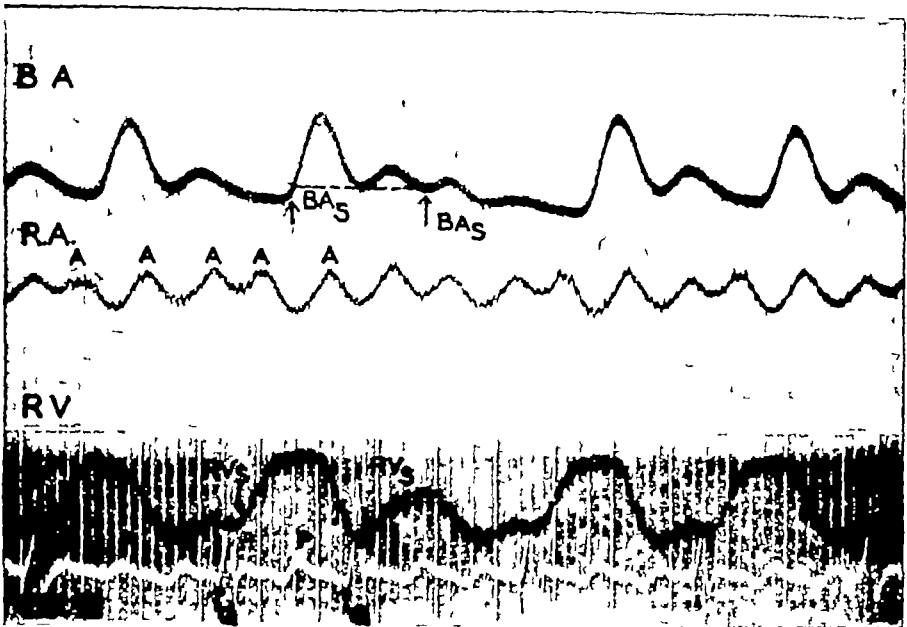
Fig 14 —Auricular flutter   Record illustrating electrical mechanical events in a case with
3 1, 2 1 A-V response
From top to bottom, blood pressure tracings in the brachial artery (B A) the right
atrium (R A), the right ventricle (R V), and electrocardiogram lead II
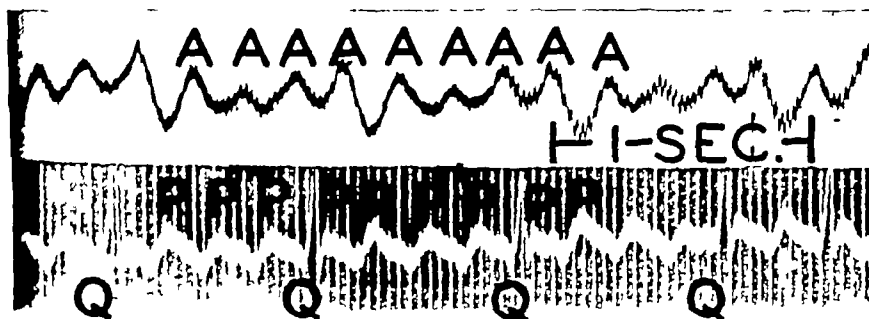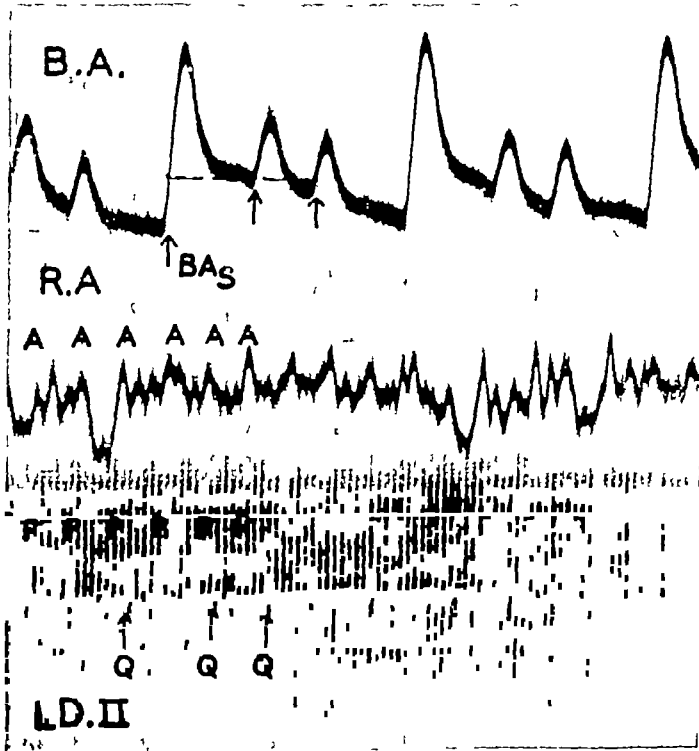

Fig 15 —Auricular flutter   Record illustrating electrical-mechanical
events in a case with 3 1, 2 1, 1 1 A-V ratio
From top to bottom, blood pressure tracings in the brachial artery
(B A), the right atrium (R A), and electrocardiogram lead II   For
discussion see text

TABLE VII

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN TWO CASES OF COMPLETE HEART BLOCK

	Case 254	Case 341
Auricular rate per minute	94	86
Ventricular rate per minute	33	33
QRS interval, sec	0·080	0·090
P–At$_s$ interval, sec	0·090	0·090
Q–RV$_s$ interval, sec	0·070	0·070
Q–BA$_s$ interval, sec	0·140	0·150
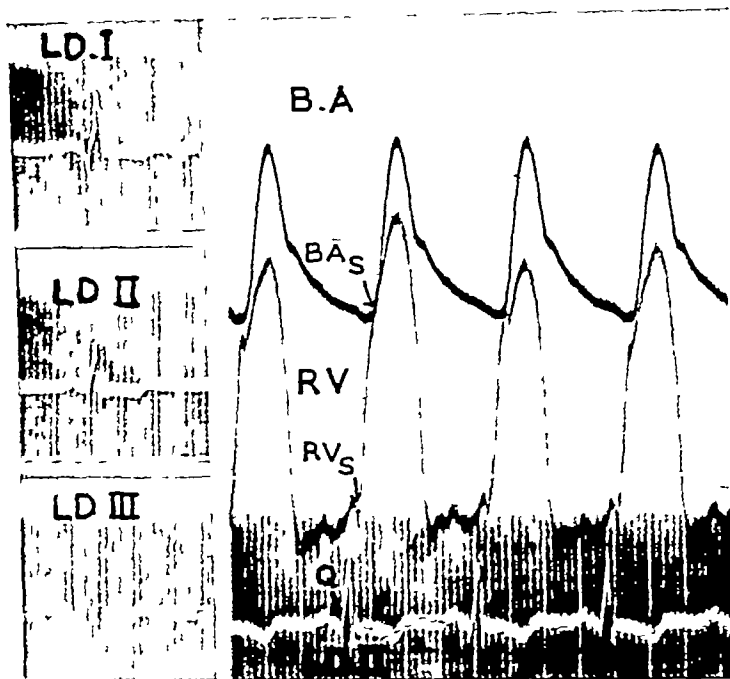
FIG 16 —Record illustrating electrical-mechanical events in a case with left bundle branch block
To the left are the standard leads of the electrocardiogram demonstrating left bundle branch block Præcordial leads showed delayed peak of R in V5 and V6 To the right, from top to bottom are blood pressure tracings in the brachial artery (B A), the right ventricle (R V) and electrocardiogram lead II For time intervals see Table VIII, Case 416, and for discussion see text

Q–BA$_s$ times were normal There was, therefore, no delay and no asynchronism in the pressure build-up of either ventricle A characteristic tracing of pressure in the right auricle may be seen in Fig 17 The striking feature was the regular sequence of auricular systoles which occurred at various times in relation to the ventricular cycles It is seen that the characteristic drop of auricular pressure during ventricular ejection took place at the expected time after the QRS complex The height of the A wave corresponding to auricular systole was variable, depending on whether or not the ventricle was in systole or diastole, i e the tricuspid valve was opened or closed, the largest deflection occurring when the tricuspid valve was closed (See the first and the last A in lower section of Fig 17) In the few instances where a P wave fell approximately 0 12 to 0 20 sec before the QRS complex, the auricular pressure tracing showed the characteristic deflection of an *a* wave followed by a *c* wave preceding the descent

RH 21 MAR '47

BA

BA

180

140

┝I-SEC┥

100

60

RA

10
5
0
-5

BA = BRACHIAL ARTERY   RA - RIGHT AURICLE
ECG = LEAD II · ALL PRESSURES IN MM HG

COMPLETE HEART BLOCK
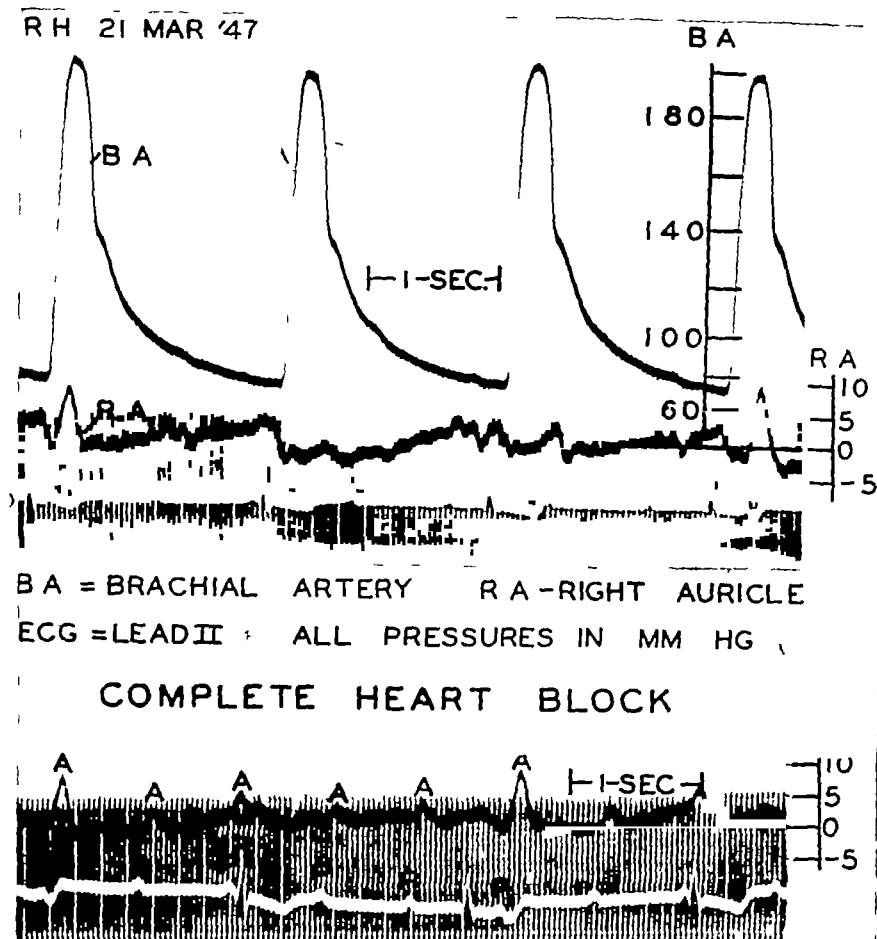
Fig 17 —Complete heart block   Records illustrating electrical-mechanical events in such a case
In the upper section from top to bottom, blood pressure tracings in the brachial artery (BA), the right atrium (RA) and electrocardiogram lead II In the lower section, blood pressure tracings in the right atrium (RA) and electrocardiogram lead II

of the base   (See the third A from the left in lower section of Fig 17)

(b) *Incomplete A-V heart block*   Incomplete A-V heart block with prolongation of the PR interval was observed in a patient with generalized scleroderma involving the heart and lungs (Fig 18)   The duration of the P wave was normal and the P–R interval was prolonged to 0 25 sec   The P–AT$_s$ time was lengthened to 0 16 sec , whereas the Q–RV$_s$ and Q–BA$_s$ times were normal, 0 08 sec and 0 14 to 0 16 sec respectively   The lengthening of the P–AT$_s$ time suggests that there was abnormality in contraction of the auricle and apparently no difficulty in conduction within the auricular muscle as

evidenced by the normal width of the P wave   In a previous publication, Cournand *et al* (1946), the prolonged Q–RV$_s$ time reported was incorrect as subsequent examination revealed the portion of the tracing read to be damped

(c) *Bundle branch block*   Ventricular asynchronism in the presence of bundle branch block has been demonstrated by several authors, using the peripheral arterial pulse wave or stethogram recorded simultaneously with the electrocardiogram   More complete data pertaining to this type of asynchronism can be added by comparison of the Q–RV$_s$ and Q–BA$_s$ times, since the former gives direct information concerning contraction of the right ventricle and
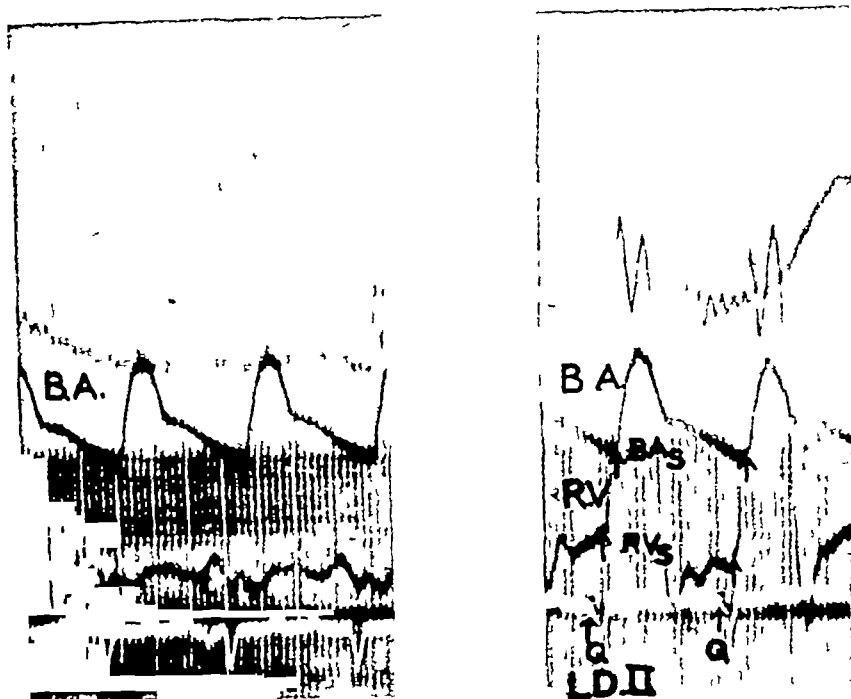
Fɪɢ 18 —Record illustrating electrical-mechanical events in a case with incomplete A–V block (prolonged P–R interval) associated with generalized scleroderma involving the heart and lungs In the section to the left, from top to bottom, pneumogram, blood pressure tracings from the brachial artery (B A), the right atrium (R A), and electrocardiogram lead II In the section to the right, pneumogram, blood pressure tracings from the brachial artery (B A), the right ventricle (R V), and electrocardiogram lead II For discussion see text

the latter indirect information concerning left ventricular contraction

(ı) *Left bundle branch block* Three patients with hypertensive and arteriosclerotic heart disease, congestive heart failure, and left bundle branch block were studied and the data is presented in Table VIII and one case (416) is illustrated in Fig 16 The time intervals in the three cases suggest a normal contraction time of the right ventricle and delayed contraction of the left ventricle, consistent with the

ventricular asynchronism expected with left bundle branch block

(ıı) *Right bundle branch block* In two cases, right bundle branch block was induced following the oral administration of 0 80 g of quinidine sulphate The electrocardiogram and blood pressure tracings, therefore, could be compared before and after the appearance of the bundle branch block The data may be found in Table IX In the first case, a 21 year old girl with an interventricular septal defect,

TABLE VIII

Rɛʟᴀᴛɪᴏɴsʜɪᴘ Bᴇᴛᴡᴇᴇɴ Eʟᴇᴄᴛʀɪᴄᴀʟ ᴀɴᴅ Mᴇᴄʜᴀɴɪᴄᴀʟ Eᴠᴇɴᴛs ɪɴ Tʜʀᴇᴇ Cᴀsᴇs ᴏғ Lᴇғᴛ Bᴜɴᴅʟᴇ Bʀᴀɴᴄʜ Bʟᴏᴄᴋ

	Case 306*	Case 261	Case 416
QRS interval sec	0 120	0 160	0 120
Q–RV$_s$ interval, sec	0·070	0 090	0 090
Q–BA$_s$ interval sec		0 220	0 240
Q–FA$_s$ interval, sec	0 200† and 0 230†		

* A case with pulsus alternans.

† Time interval variation corresponding to strong and weak beats of pulsus alternans (see text)

c

TABLE IX

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN RIGHT BUNDLE BRANCH BLOCK

Right Bundle Branch Block induced by Quinidine

	Case 333		Case 351	
	Control	R B B Bl	Control	R B B Bl
QRS interval, sec	0 060	0 120	0 105	0 120
Q–RV$_s$ interval, sec	0 070	0 110	0 070	0 110
Q–BA$_s$ interval, sec	0 170	—	0 190	0 190

Right Bundle Branch Block in Cases with Arteriosclerotic Heart Disease and Cor Pulmonale (Case 440) and with 2 1 A-V Block (Cases 302 and 268)

	Case 440	Case 302	Case 268
QRS interval, sec	0 140	0 160	0 170
Q–RV$_s$ interval, sec	0 130	0 120	0 105
Q–PA$_s$ Interval, sec	0 150	—	—
Q–BA$_s$ interval, sec	0 130	0 170	0 240

the control tracings showed normal electrical complexes and time intervals   After quinidine, a right bundle branch block developed and the normal Q–RV$_s$ time of 0 070 sec was prolonged to 0 110 sec   In the second case, a 60 year old man with arteriosclerosis and an old myocardial infarct, the control electrocardiogram showed evidence of myocardial damage and early incomplete bundle branch block, characterized by a QRS of 0 105 sec in lead II and a delayed peak of the R wave over the left præcordium   Before administration of quinidine, the Q–RV$_s$ time was normal but the Q–BA$_s$ time was slightly prolonged, confirming the electrocardiographic diagnosis of early incomplete left bundle branch block   After quinidine, an S wave appeared in lead I and the QRS complex increased in that lead to 0 120 sec   The Q–BA$_s$ time remained unchanged but the Q–RV$_s$ time increased from 0 070 sec to 0 110 sec (Fig 7)   In Fig 19 (Table IX, Case 440) is illustrated an additional case of right bundle branch block observed in a patient with arteriosclerotic heart disease and cor pulmonale, in which a markedly prolonged Q–RV$_s$ time is seen

In summary, intracardiac and intra-arterial blood pressure tracings recorded simultaneously with the electrocardiogram demonstrated clearly the presence of ventricular asynchronism in bundle branch block

These findings confirm and add to the observations of various authors (Castex *et al*, 1941, Battro *et al*, 1936, Katz *et al*, 1927 and 1935, Kossman *et al*, 1947, Nichol, 1933, and Wolferth *et al*, 1935) who have studied mechanical and electrical relationships in bundle branch block   Various types of simultaneous tracings were employed by these authors

and include electrocardiograms, peripheral artery blood pressure tracings, and in a few instances stethograms, phlebograms, and apical cardiograms   They found that in left bundle branch block there was a prolongation of the " ejection time " which corresponded to the prolongation of the Q–BA$_s$ time found in the present study   In right bundle branch block the " ejection time " remained essentially normal   Data concerning the events in the right ventricle was obtained by indirect means and is subject to interpretation

(*d*) *Right bundle branch block with incomplete 2 1 A-V block*   In 2 patients a 2 1 A-V block was associated with right bundle branch block   In addition, one of these patients had short periods of complete heart block   The data in these two cases may be found in Table IX   In the first case the duration of the QRS complex was 0 160 sec, the ventricular complexes were of the aberrant type with downward deflection in lead I and upward deflection in lead III, suggesting that the stimulation arrived first in the left ventricle   The Q–RV$_s$ time was significantly prolonged to 0 120 sec while the Q–BA$_s$ time was normal (0 170 sec)

In the second case (Fig 20 and 21 and Table IX, Case 268) during the periods of incomplete 2 1 heart block the P–R interval was markedly prolonged to 0 310 sec   The Q–RV$_s$ and Q–BA$_s$ times were both lengthened to 0 105 and 0 240 sec, respectively   During the period of complete heart block with an auricular rate of 71 and a ventricular rate of 27, the ventricular complexes were of the same aberrant configuration and the same duration, again with downward deflection in lead I, upward in lead III
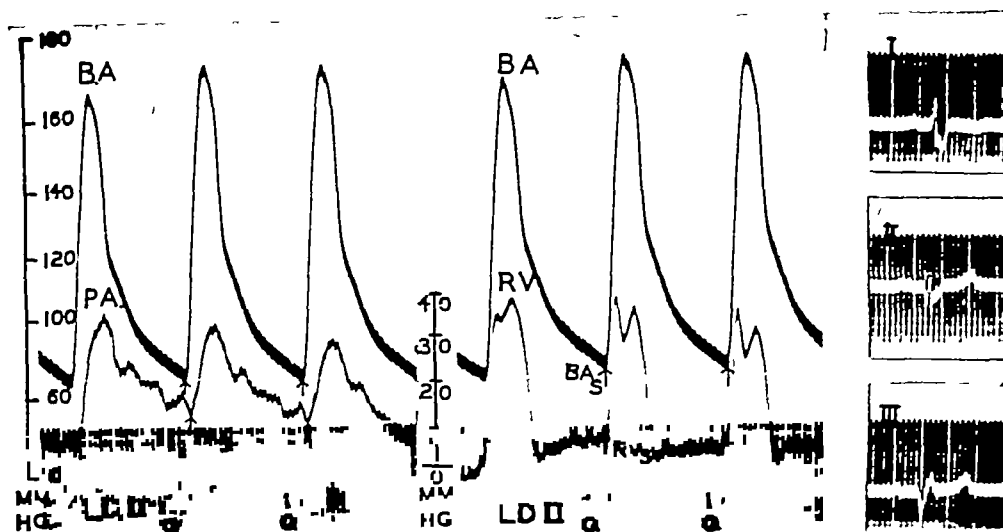
FIG 19 —Records illustrating electrical-mechanical events in a case with right bundle branch block.
    To the right, are the standard leads of the electrocardiogram demonstrating right bundle branch block   In the centre, are blood pressure tracings in the brachial artery (B A.), the right ventricle (R V), and electrocardiogram lead II   To the left, are blood pressure tracings in the brachial artery (B A), the pulmonary artery (P A), and electrocardiogram lead II
    Note, as in Fig 3, the ascending slopes of the right ventricle and pulmonary artery do not coincide   For figures see Table IX, Case 440   For discussion see text

FIG 20 —Records illustrating electrical mechanical events in a case with right bundle branch block and 2 1 A-V block
    From top to bottom, blood pressure tracings in the brachial artery (B A) the right atrium (R A), and electrocardiogram lead II
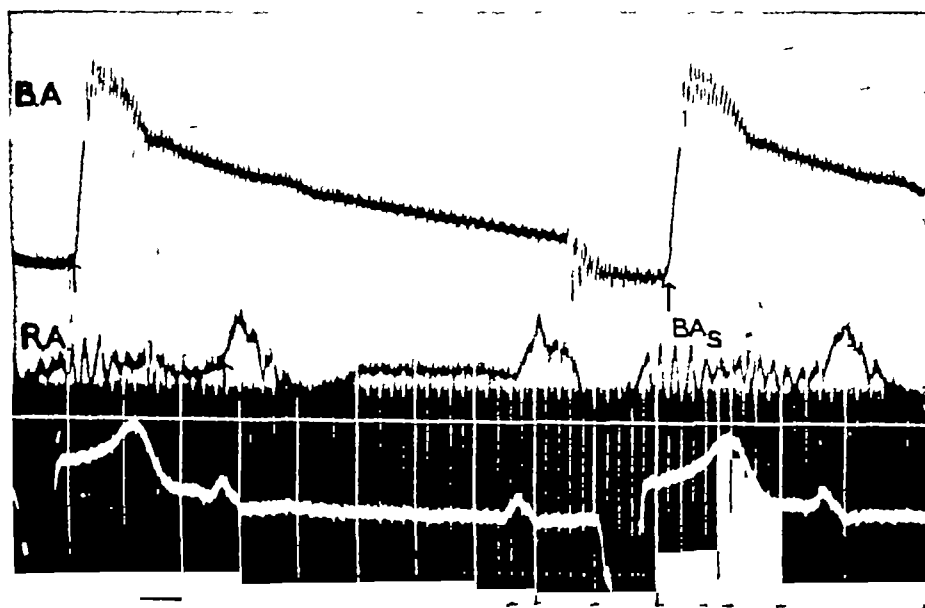   For data see Table IX, Case 268, and for discussion see text
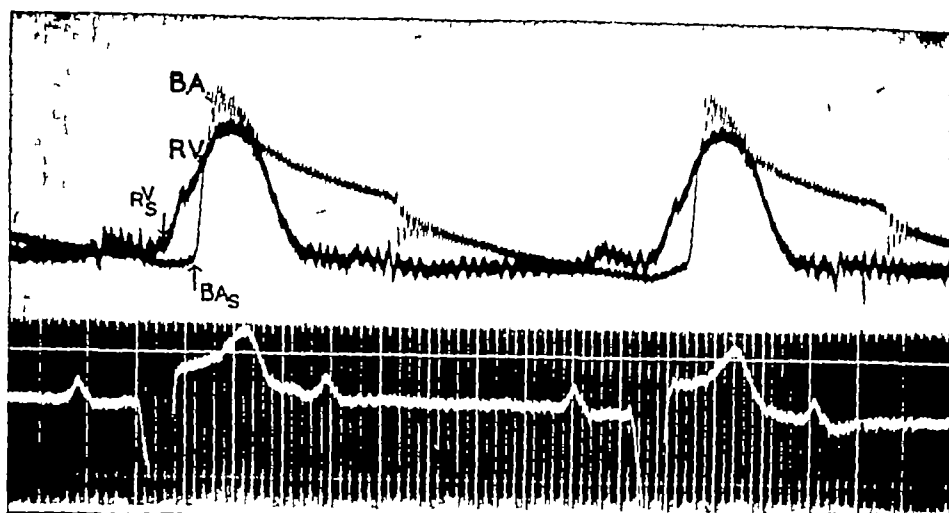
FIG 21 —Records illustrating electrical-mechanical events in a case with right bundle branch block and 2 1 A-V block.

From top to bottom, blood pressure tracings in the brachial artery (B A), the right ventricle (R V), and electrocardiogram lead II

For data see Table IX, Case 268, and for discussion see text

This suggests that ventricular depolarization was the same as during incomplete A-V block, and that the idioventricular focus was probably in the His bundle The Q-RV$_s$ and Q-BA$_s$ time intervals were unchanged During both complete and incomplete A-V block the duration of P-AT$_s$ time was short (0 050 sec), see Fig 20, indicating no abnormality of auricular contraction, in contrast to the findings in the case with incomplete A-V block previously described

These two patients are of particular interest because during a period of 2 1 block with right bundle branch block the electrocardiographic patterns were identical In the first case there was a delay in right ventricular contraction, whereas in the second case slow spread of stimulation or delay in contraction existed in both ventricles

(6) Pulsus Alternans

One case of hypertensive and arteriosclerotic heart disease with left bundle branch block showed evidence of pulsus alternans of the mechanical type The findings in this case (306) are illustrated in Fig. 22 and the data listed in Tables VIII and X In the femoral artery tracings there was a variation in the systolic peak which occurred in a regular manner and may be interpreted as a succession of strong and weak beats In contrast there was a steady level of the systolic peaks in the right ventricle There was no evidence in the electrocardiogram of electrical alternation The duration of the QRS complex in alternate beats remained the same and the Q-RV$_s$ time also did not vary The striking abnormality was the rhythmic variation of the Q-BA$_s$ time This interval was shorter for the beat corresponding to the high systolic peak and longer for the beat corresponding to the lower systolic peak These variations in pressure as well as the variations in the Q-BA$_s$ time, occurring rhythmically without any variation in the duration of the QRS complex, suggest a less efficient ventricular contraction every other beat However, it is not possible to eliminate

TABLE X

RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS IN PATIENT WITH PULSUS ALTERNANS (CASE 306)

	Strong beat	Weak beat
QRS interval, sec	0 120	0 120
Q-RV$_s$ interval, sec	0·070	0 070
Q-FA$_s$ interval, sec	0 200	0 230

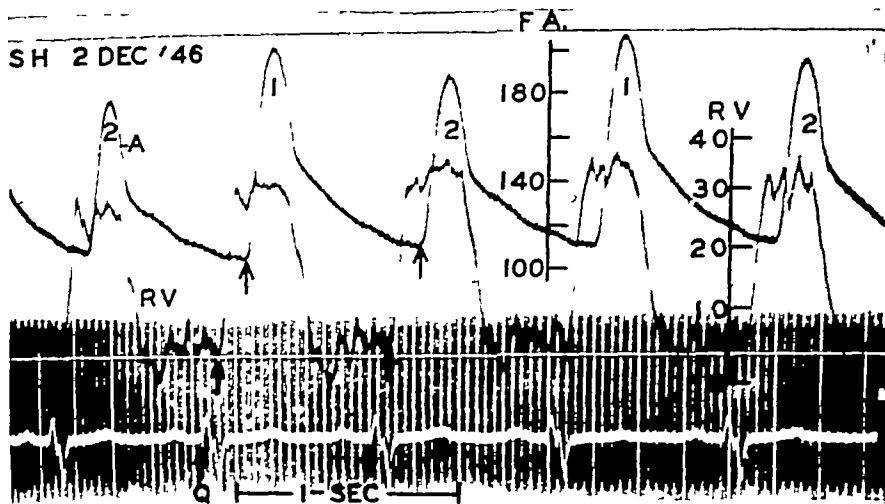FIG 22 —Pulsus alternans   Records illustrating electrical-mechanical events in such a case
From top to bottom, blood pressure tracings in the femoral artery, the right ventricle,
and electrocardiogram lead II   No 1 corresponds to the strong beat and No 2 to
the weak beat
Note absence of alternation of pressure in right ventricle   For data see Tables
VIII and X, Case 306, and for discussion see text
F A = Femoral artery   R V = Right ventricle   All pressures in mm Hg
Electrocardiogram, lead II

as a factor rhythmic variation of peripheral vascular tone of reflex origin, which would ultimately influence the curve of blood ejection from the left ventricle into the aorta and the pulse wave velocity

SUMMARY AND CONCLUSIONS

The relationship between electrical and mechanical events in the cardiac cycle was studied in normal subjects, in children with congenital heart disease, and in adults with cardiovascular disease

In children the intervals were shorter than those of normal adults   The prolongation of the isometric contraction of the right ventricle in children with congenital heart disease seemed to be dependent upon hypertension of the lesser circulation

In adults with heart disease who had normal sinus rhythm and no conduction abnormalities, the time intervals were identical with those found in normal adults unless they were in congestive failure with hypertension of the lesser circulation   In this event the Q-PA$_s$ time interval was slightly prolonged and the duration of isometric contraction of the right ventricle was also longer than normal

Abnormalities of rhythm, conduction, and contraction encountered in patients with cardiovascular disease were also analysed and the following points deserve emphasis

(a) Ventricular premature contractions apparently produce two types of asynchronism with a lag in one or the other ventricle   It is difficult to interpret the relationship between electrical configuration of the premature contractions and the mechanical events, since premature beats with electrocardiographic patterns identifying them as arising from opposite ventricles produced the same type of ventricular asynchronism

(b) In chronic auricular fibrillation, in addition to the complete arrhythmia, disturbances of the contraction mechanism of both ventricles were present

(c) In auricular flutter the time intervals remained constant and normal during pure flutter with a constant A-V ratio   Minor variations in the Q-RV$_s$ and Q-BA$_s$ intervals as well as variations in right ventricular and brachial artery systolic pressures were found when the degree of block varied

(d) In cases of complete heart block with bundle of His ventricular rhythm the auricular and ventricular electrical-mechanical intervals remained normal even though the conduction defect consisted of complete A-V dissociation   In uncomplicated bundle branch block ventricular asynchronism of the expected type was found   However, in one patient with both incomplete 2 1 A-V block and right bundle branch block there was a delay in onset of the mechanical systole in both ventricles

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R WAVES INTERRUPTING T WAVES

BY

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In the course of some experiments on anæsthetized dogs and cats concerned with the production experimentally of ventricular flutter and ventricular fibrillation, Fastier and Smirk (1948) noted that R waves sometimes appeared on the descent of the antecedent T waves, shortly before the onset of ventricular flutter   The flutter was induced by a substance amarin * which had been found by one of us (F H S) to alter the response of the animals to adrenaline so that a moderate dose of adrenaline, ordinarily well tolerated, would now give rise to ventricular flutter

These observations led me to seek more closely for such phenomena in human electrocardiograms The present paper concerns 17 patients in whom R waves have been observed on the T waves of antecedent complexes   It seems that interruptions of T waves by R waves are not very uncommon, are likely to prove important prognostically, and seem to provide an indication for treatment

Little has been written on this subject either from the experimental or from the clinical standpoint, and such information as is available may be unfamiliar to some of the authors who have published records without commenting upon the phenomenon The first reference I was able to discover to the occurrence of an R wave on a T wave was in a footnote by Katz (1928) in the course of his comprehensive review on the T wave   Katz mentioned here that an example of an R wave on a T wave has been observed by Dr Ashman, three examples by Drs Feil and Seigel, and three by himself   He mentioned that the only published record was by Wenkebach and Winterberg (1927) and that Wiggers had seen it in dogs   I have been unable to find any record of subsequent reports on the finding of R waves on the T waves with the exception of Scherf

* C₆H₅—CH—NH
  | \\
                         C—C₆H₅
  C₆H₅—CH——N   /

and Boyd (1940) and of Ashman and Hull (1941) in their books on electrocardiography, they confine themselves to the statement that an R wave may encroach on the descent of the T wave

The published electrocardiograms show many examples in which R waves appear to arise on the descent of T waves but, with the exception referred to above, I have found so far no corresponding comment by the authors

Theoretically R waves might occur superimposed upon T waves in several ways   Most of these theoretical possibilities have been given practical illustration in the 17 cases here reported

(1) A ventricular complex of supraventricular origin could be interrupted by another ventricular complex of supraventricular origin (Cases 3, 4, 13, 14, 15, 16, Fig 3 and 9)   This might occur in auricular paroxysmal tachycardia   in auricular fibrillation (Fig 3 and 9), in auricular flutter, and possibly with very premature auricular systoles

(2) A ventricular complex of supraventricular origin could be interrupted by a premature ventricular complex (Cases 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 15, 17, Fig 6 and 7)

(3) A premature ventricular complex could be interrupted by a ventricular complex of supraventricular origin (Case 4, Fig 4)

(4) A premature ventricular complex could be interrupted by another premature ventricular complex (Cases 1, 2, 4, 5, 7, 8, Fig 1, 2, 4, 5, and 8) This last might occur with single pairs of ventricular premature beats (Fig 1) or in the course of ventricular paroxysmal tachycardia (Fig 2)

Reference to published cardiographic tracings illustrating a variety of cardiological conditions suggests that some of the other theoretical possibilities may have been realized   For example interruptions of paroxysmal auricular tachycardia (Graybiel and White, 1946) in which the P waves appeared in the S–T segments

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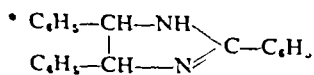
CASE REPORTS

Case 1, male, aged 59 years   Retrosternal pain twelve hours before admission   The electrocardiographic diagnosis was that of *anterior apical infarction*   In two instances in about 46 seconds of electrocardiographic recording examples were found of an ectopic ventricular complex interrupted before its completion by a subsequent ectopic complex (Fig 1)   Both interruptions occurred on the latter half of the T wave

The patient was improving during the first 19 days and then had an extension of the cardiac infarction with a further fall in the blood pressure Next day he was noticed to be breathing stertorously   Shortly after he tried to sit up and died suddenly, as was thought, from ventricular flutter The autopsy revealed multiple small infarcted areas in the anterior apical region

Case 2, male, aged 46 years   *Cardiac infarction* Severe retro-sternal pain of 36 hours duration About one month after admission the patient developed a *ventricular paroxysmal tachycardia* and was treated by quinidine which restored a natural regular rhythm   The patient was discharged in good condition

The electrocardiograms were indefinite in regard to the clinical diagnosis of cardiac infarction   The terminal deflection of the first run of tachycardia
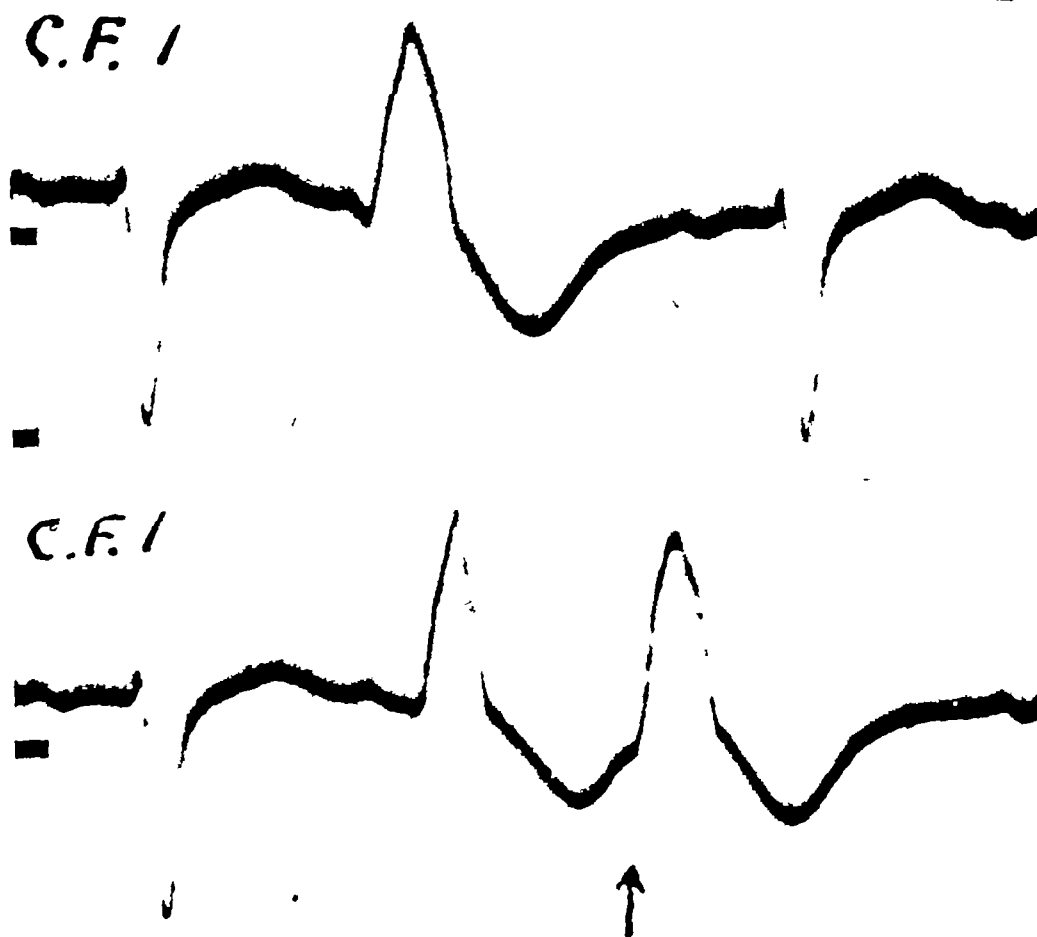
FIG 1 —Case 1   The upper trace shows a single uninterrupted premature ventricular systole and the lower shows a pair of premature ventricular systoles of which the second interrupts the terminal deflection of the first   The interrupted complex may be compared in shape with the complete complex in the upper trace and with the complex that follows it   Time intervals 0 1 sec

in lead III and the ventricular complex towards the end of the lead III strip indicate the shape and duration of uninterrupted ventricular complexes (Fig 2) In the middle of the paroxysm the individual complexes differ in duration and this seems to depend chiefly on the point at which the T-like terminal
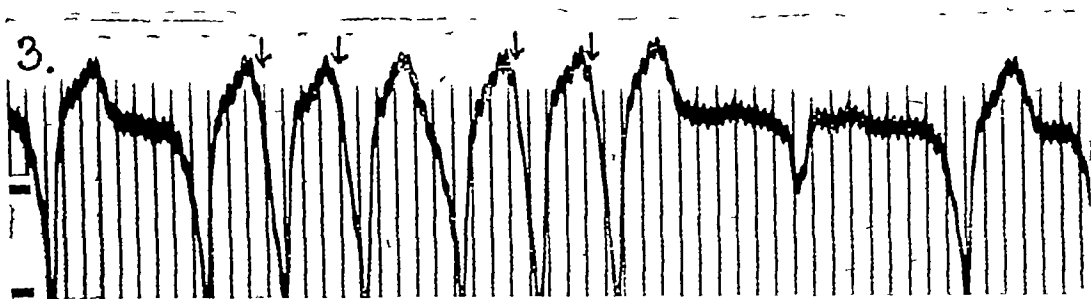
FIG 2—Case 2 The trace shows a paroxysm of ventricular tachycardia This complex at the end of the paroxysm and the complexes at the extreme left and right of the trace are uninterrupted The arrows mark the points where complexes are interrupted during the paroxysm Comparison with intact complexes indicates how much of the interrupted complexes have been cut off by the beginnings of new ventricular complexes Time intervals 0·05 sec
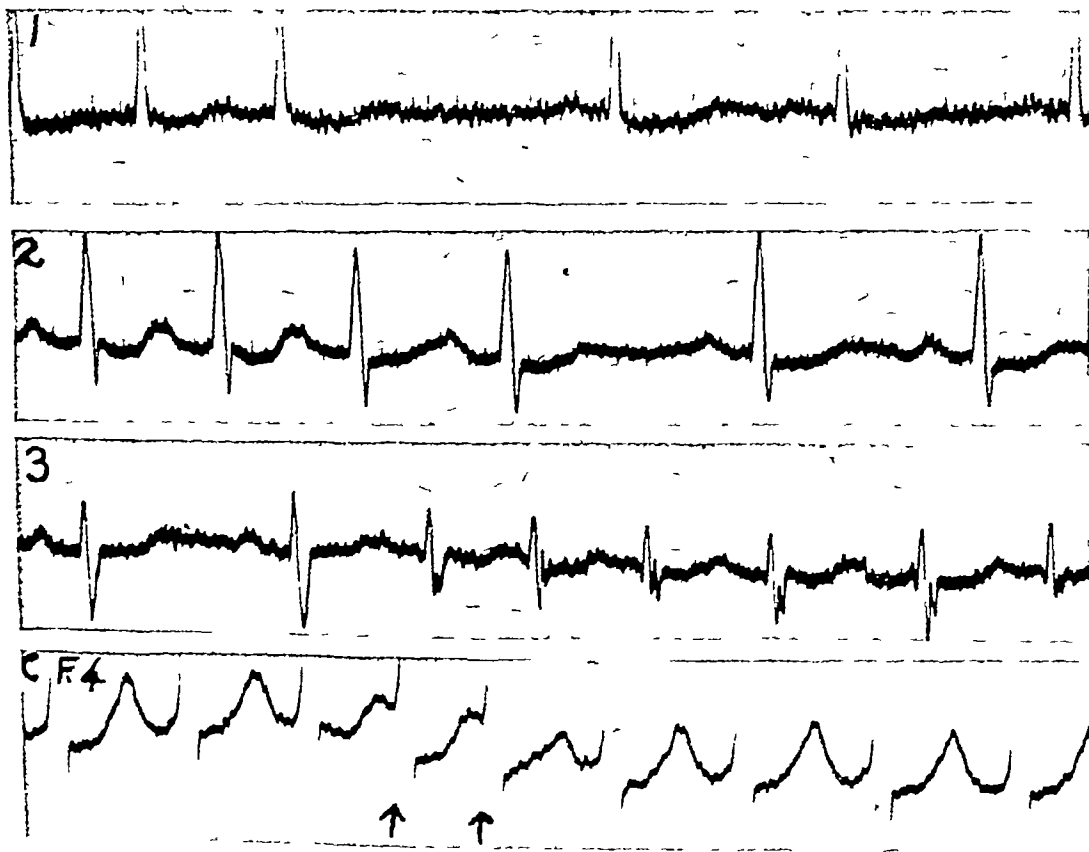
FIG 3 —Case 3 Lead I shows the end of a period of rapid beating with the return of sinus rhythm, lead II shows an end of rapid beating and lead III the beginning of rapid beating with polymorphic ventricular complexes of supraventricular origin. The irregular arrhythmia has been called paroxysmal auricular fibrillation CF4 shows two interruptions by R waves of the antecedent T waves Time intervals 0·05 sec

D

deflection of a complex is interrupted by the initial sharp downward deflection of the next complex

Case 3, male, aged 56 years   *Myocardial degeneration and thyrotoxicosis   Paroxysmal supraventricular tachycardia probably auricular fibrillation* Admitted with breathlessness on exertion, of 6 months' duration   Thyroidectomy was followed by improvement in the physical condition   The basic rhythm is regular and of sinus origin   At times there is an irregular tachycardia with ventricular complexes which do not differ greatly from those found when the rhythm is regular (Fig 3) The irregular rhythm is associated with variations in the shape of the ventricular complexes which, however, are supraventricular in origin   It is not possible entirely to eliminate multiple premature auricular systoles as a cause for the tachycardia but auricular fibrillation seems more likely

Case 4, male, aged 71 years   *Myocardial degeneration, auricular fibrillation, multiple premature ventricular systoles*   Admitted to hospital because of a confused mental state   He was reasonably active for his years   Irregular rhythm due to auricular fibrillation and short runs of paroxysmal ventricular tachycardia   Interruptions of T waves by R waves occur frequently   Some of these are

interruptions of ventricular complexes of supraventricular origin by premature ventricular complexes, others are of premature ventricular complexes by other premature ventricular complexes (Fig 4A) Instances were observed of the interruption of a premature ventricular complex by a ventricular complex of supraventricular origin (Fig 4 A and B) and of a ventricular complex of supraventricular origin by another ventricular complex of supraventricular origin

Case 5, male, aged 71 years   *Myocardial degeneration, auricular bigeminy, sinus bigeminy, multiple premature ventricular systoles*   Admitted because of a right-sided inguinal hernia and found to have cardiac irregularity   In the last four months before admission there had been shortness of breath on exertion but no swelling of the ankles   (See Fig 5)

Case 6, male, aged 58 years   *Cardiac infarction* Electrocardiograms showed a cardiac infarction and multiple premature ventricular systoles with interruptions of T waves by R waves (Fig 6)

Case 7, female, aged 40 years   *Myocardial damage of unknown origin, multiple premature systoles* Numerous examples of ventricular premature systoles interrupting beats of normal sinus origin
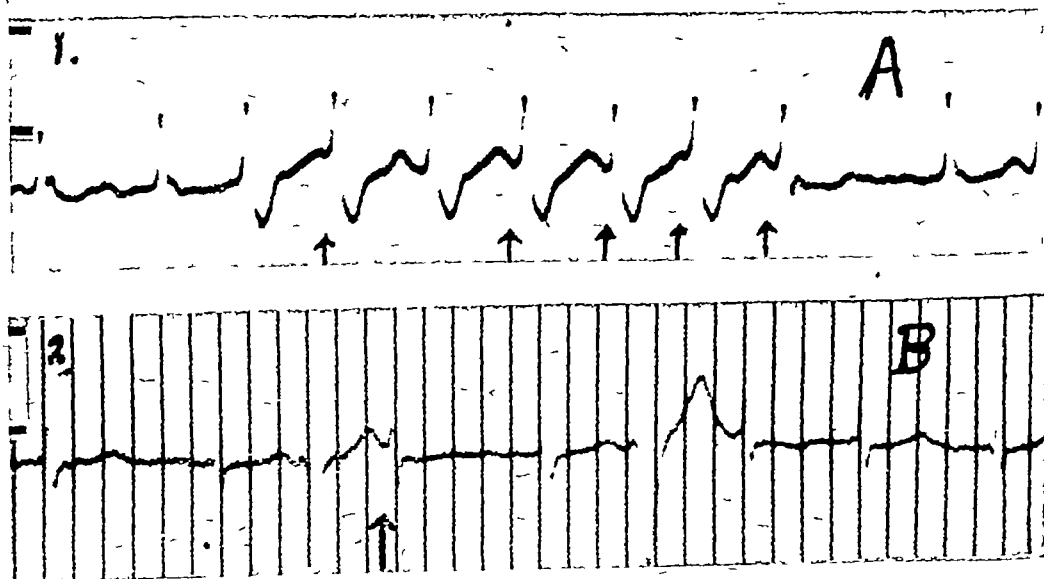
FIG 4 —Case 4
(A) Auricular fibrillation   The trace shows a run of six premature ventricular systoles followed by what appears to be a ventricular complex of supraventricular origin interrupting the T wave of the last premature ventricular systole
(B) Auricular fibrillation   The trace shows the T wave of a premature ventricular complex interrupted by a ventricular complex which is clearly of supraventricular origin.   Time intervals 0 1 sec

FIG 5.—Case 5

(A) The upper trace is an electrocardiogram recorded by a Matthews' oscillograph and shows auricular bigeminy broken by premature ventricular systoles which occur in two groups, each of three ventricular complexes The 1st and 2nd premature ventricular systoles in each group are interrupted respectively by the 2nd and 3rd premature ventricular systoles The shape of the uninterrupted 3rd systoles shows that the 1st and 2nd systoles are incomplete The ballistocardiographic trace, using Malcolm's instrument, indicates a much smaller output of the heart from the premature than from natural systoles Time trace 0 2 sec

(B) The lower trace is a heart sound record and the lower trace a simultaneous lead II electrocardiagram, both taken using a pair of Matthews' oscillographs The latter shows a supraventricular bigeminy with wandering pacemaker and two premature ventricular systoles of which the second interrupts the first. The heart sounds alternate in intensity during the bigeminy, the louder sound following the longer diastole The premature ventricular systoles give rise to weaker heart sounds The second premature systole leads to a second heart sound. This raises the question of whether some filling of the heart took place between the two premature ventricular beats. Time trace 0 2 sec.

FIG 6.—Case 6   The trace shows the interruption of a complex of sinus origin by a ventricular premature systole at the point marked with an arrow   Time intervals 0·05 sec

FIG 7 —Case 7   The trace shows interruptions of the T waves of complexes of sinus origin by the R waves of premature ventricular systoles   Time intervals 0 1 sec

(Fig 7)   Examples were also encountered of polymorphic ventricular premature systoles interrupting other premature ventricular systoles   Apart from the numerous premature beats the electrocardiogram would have passed as normal

Case 8, male, aged 77 years   Cardiac asthma, general congestive heart failure, benign arterial hypertension   Shortness of breath on exertion for two years, swelling of the ankles for one month, and extreme nocturnal breathlessness for four days prior to admission   The blood pressure was 220/108   The basic rhythm, of sinus origin, was interrupted by frequent polymorphic premature ventricular systoles occurring at various times after the antecedent complexes   Interruptions of T waves by R waves were frequent (Fig 8)

attack of pain which woke him in the early morning and continued for some hours in the absence of physical exertion, no other clinical evidence of recent cardiac infarction   Cardiograms suggested an old myocardial infarction but no recent damage   the T wave was inverted in leads I and IV, and in lead III there was a premature ventricular systole interrupting the T wave during its descent (no other abnormality and regular rhythm with normal P-R interval)

Case 11, male, aged 79 years   Recent cardiac infarction   This patient began with vomiting, and pain in the chest   He was obviously very ill and cyano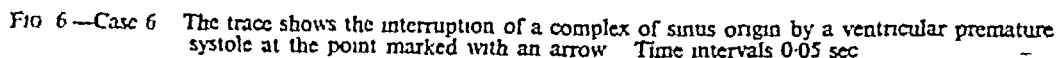sed, his condition deteriorated and he died   Cardiograms show a basic sinus rhythm with normal P-R interval interrupted by numerous premature

FIG 8 —Case 8   The trace shows interruption of the terminal deflection of an ectopic ventricular complex by the initial deflection of another ectopic ventricular complex   Time intervals 0 1 sec

Case 9, male, aged 63 years   Posterior basal infarct   One month after the onset of the infarction, the patient, apparently well on the way to recovery, was telling the ward sister how well he felt and suddenly dropped back dead, apparently from ventricular flutter or fibrillation   The autopsy revealed a posterior basal cardiac infarction   Cardiograms showed interruption of ventricular complexes of supraventricular origin by ectopic ventricular complexes   The premature beats occurred at varying intervals after the previous beats but were not polymorphic

Case 10, male, aged 77 years   Angina of effort, old cardiac infarction   Admitted because of an

ventricular systoles   The QRS-T complexes were approximately 0 1 sec in duration   There was a 6 mm Q wave in lead III with a sharply inverted T wave   A clear interruption of the T wave of a complex of sinus origin by an ectopic ventricular complex occurred in lead I

Case 12, male, aged 77 years   Myocardial degeneration   Short of breath and unable to hurry on level ground for six years prior to admission   Signs of congestive heart failure were minimal   Sinus rhythm, but premature ventricular systoles occurred at fairly frequent intervals and several quite distinct interruptions of complexes of supraventricular origin by ectopic ventricular complexes occur

Case 13, female, aged 78 years *Cardiac asthma, auricular fibrillation, hypostatic pneumonia* Admitted with severe breathlessness which was thought to be the result of cardiac asthma In hospital she developed a hypostatic pneumonia and died Auricular fibrillation QRS–T complexes of supraventricular origin sometimes occurred sufficiently early to interrupt the antecedent T wave of other supraventricular complexes about half-way down their descents

Case 14, female, aged 70 years *Acute exacerbation of chronic bronchitis, congestive heart failure, auricular fibrillation* The blood pressure was 180/80 The congestive failure was treated by digitalis, the bronchitis improved, and the patient was discharged in fair condition Auricular fibrillation in CF2 and CF4 distinct interruptions of complexes of supraventricular origin by other complexes of supraventricular origin occurred There was great variation in the shape of the ventricular complexes

Case 15, female, aged 73 years *Auricular fibrillation* Auricular fibrillation and interference with conduction in the branch bundles Complexes of supraventricular origin were interrupted on occasion by other complexes of supraventricular origin and at times by ectopic ventricular complexes

Case 16, female, aged 66 years *Paroxysmal auricular fibrillation* In two instances R waves were present on the descent of the antecedent T waves

showed a basic sinus rhythm, the ectopic ventricular complexes were polymorphic but falling, in regard to shape, into two main types of which one type only gave rise to interruptions of the T waves of sinus beats

FINDINGS IN THESE CASES

The principal features of the 17 cases recorded with R waves interrupting T waves are set out in Table I Most patients were in the later years of life, ten being over 70 and seven between 40 and 69 There was a preponderance of males Thirteen exhibited premature ventricular systoles, in one of these, only a single premature ventricular systole was present in the short length of tracing available, in the remaining 12 two or more ventricular premature systoles occurred, in tracings taken with the same lead, and the premature beats were polymorphic in 11 cases (Fig 7 and 8) Of these 12 cases, 11 showed premature beats starting at irregular intervals of time after the antecedent normal beats In the remaining case there were only two premature ventricular complexes and a conclusion as to whether the time interval was constant or variable could not be reached Of the 12 cases with more than one premature systole 8 showed examples of pairs of premature beats occurring together Some of these showed groups of three together and 3 of the 8 showed runs of paroxysmal tachycardia of five or more complexes (Fig 2) In two of the cases where no such pairing of the ventricular premature systoles was discovered a considerable length of tracing was
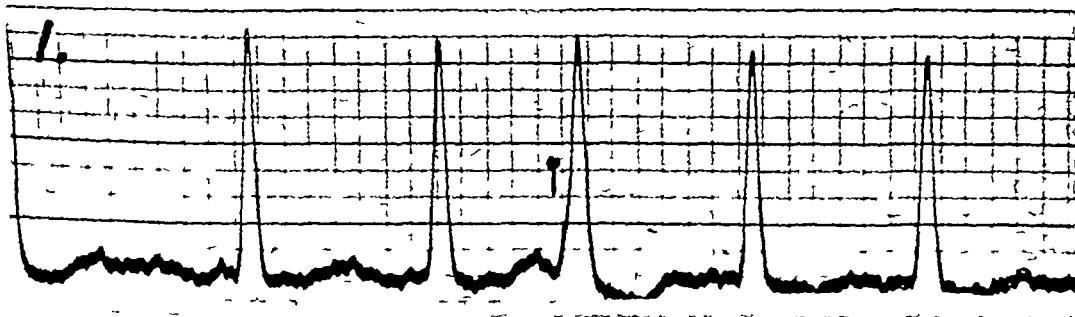
FIG 9 —Case 16 Auricular fibrillation. T wave interruption Time intervals 0 05 sec

(Fig 9) The QRS–T complexes showed variations in shape There were no premature ventricular systoles

Case 17, female, aged 62 *Melancholia, multiple premature systoles* Admitted for electrical convulsive therapy on account of mental depression, hallucinations, and delusions Electrocardiograms

available and it seems likely that pairing of the beats was not occurring in these cases In the other two cases only short lengths of tracing were available and pairing may or may not have been present at other times

There were six cases with auricular fibrillation and it is interesting that all six showed polymorphic ventricular complexes of supraventricular origin

(Fig 3) This polymorphism is not usual in ordinary cases of auricular fibrillation and would appear to be a feature of cases in which R waves appear upon T waves. Two of the six cases with auricular fibrillation also exhibited ectopic ventricular systoles and these also exhibited polymorphism. It was noted, but only when finally analysing the results, that three out of the six cases with auricular fibrillation (Fig 3) sometimes showed sinus rhythm, this seems to be a higher proportion of paroxysmal auricular fibrillation than one would expect to encounter in a random collection of auricular fibrillation cases. From the above paragraphs it will be seen that in the 16 cases where it was possible to examine the phenomenon, polymorphism occurred in 15, being manifest either in ectopic ventricular complexes or in ventricular complexes of supraventricular origin or in both of these

The four types of interruption that should occur theoretically have been found in the present series. Five patients were found in whom ventricular complexes of supraventricular origin interrupted other ventricular complexes of supraventricular origin and in one additional patient this probably occurred. These were also patients with auricular fibrillation and no such interruption occurred in any of the patients with sinus rhythm. Interruption of ventricular complexes of supraventricular origin by ectopic ventricular complexes (Fig 6) and of ectopic ventricular complexes by other ectopic ventricular complexes (Fig 1 and 4) both occurred fairly frequently, there being 9 patients who definitely, and three more who probably, exhibited the former phenomenon, and six patients who definitely exhibited the latter. Only one patient showed ectopic ventricular complexes being interrupted by ventricular complexes of supraventricular origin (Fig 4) and this, as might be expected, was in a patient with both auricular fibrillation and multiple ectopic ventricular systoles

One patient exhibited four types of interruption. Two patients exhibited two kinds of interruption and three patients probably had two types of interruption

EVIDENCE OF INTERRUPTION OF T WAVES BY R WAVES

Some examples of the interruption of T waves by R waves have been presented. It may be considered that there has been an unmistakable interruption when a ventricular complex of well-defined shape has its latter end cut off by the premature development of an R wave. In most cases complete ventricular complexes can be discovered which, up to the point of interruption, are identical with the interrupted complex, and a comparison of the complete and interrupted complexes makes it quite clear that there has been an interruption (Fig 1). The distance between the R wave of the interrupted complex and the R wave of the interrupting complex, ordinarily, will be less than the length of the complete QRS-T complex. In patients who show the more striking interruptions of T waves by R waves there are usually in addition a large number of interruptions which, however, are not so convincing—those where the R wave arises low down on the descent of the T wave, those where extra cardiac potentials by deflecting the isoelectric base line are altering the shape of the complexes, and those where the interruption appears to be due to a prolongation of the interrupted QRS-T complex as much as to prematurity of the R wave

OTHER FEATURES OF CASES R WAVES ON T WAVES

Several of the examples of R waves on T waves have been encountered in cases of cardiac infarction especially about the end of the first week and the interruptions then are caused by premature ventricular systoles (Fig 1 and 6)

In cases which are not cardiac infarctions a variety of clinical conditions have been associated with the appearance of R waves on T waves. Most of these patients show evidence of substantial myocardial damage. In addition, there is a similarity in the electrocardiographic features of all these cases which is not merely accidental

(1) In 11 out of 12 cases, the ectopic ventricular complexes show variations in the shape (polymorphism). These variations in shape, however, are encountered not only when the premature ventricular systoles arise, as is usual in these patients, from multiple ectopic foci but also among ventricular complexes which arise in response to stimuli of supraventricular origin (Fig 3)

(2) Ectopic ventricular beats often occur in pairs or triplets or in runs of ventricular paroxysmal tachycardia

(3) The distances between premature beats and their antecedent normal complexes were variable. When pairs of ventricular premature systoles occur together, the distance between the two members of a pair is also a variable

As will be seen later, the above changes may indicate increased excitability of the myocardium

The recognition of the fact that cases exhibiting interruptions of T waves by R waves commonly showed the above features, has led to a more careful, and often fruitful, search for interruptions, more particularly in cases where (a) ventricular complexes are polymorphic and at variable intervals after the antecedent beat, (b) the heart rate is fast and

irregular, and (c) where some of the R waves arise close to the descending limb of the T wave *

THE REFRACTORY PERIOD OF CARDIAC MUSCLE

The presence of R waves on T waves indicates that a new wave of excitation may arise within the heart before the previous wave of excitation has ended   This statement has reference to the heart U wave   In the course of some observations with Mr Fastier, direct leads from the surface of the heart have been taken in the dog in the course of the experimental production of ventricular flutter by the administration of amarin followed by adrenaline In the stage preceding the onset of ventricular flutter we have observed interruption of the terminal deflection of these (direct lead) electrograms (Fig 10)
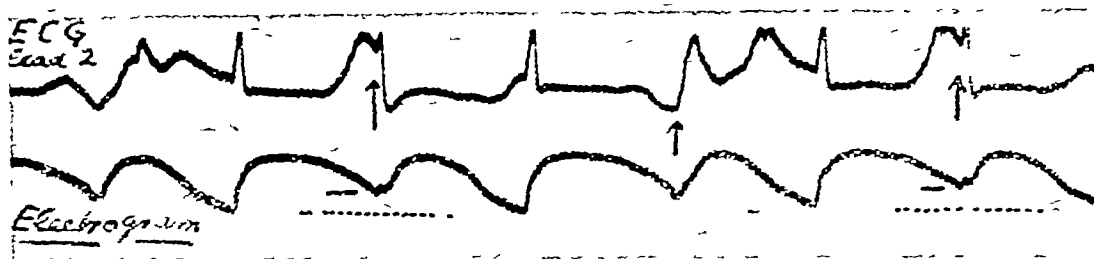

FIG 10—Dog (17 kg 6 3 g), under sodium barbitone   Vagi intact.   The upper trace is an electrocardiogram which shows R waves appearing on T waves just before the onset of ventricular flutter, which was induced with adrenaline (25 μg) following treatment with amarin
   The lower trace is a simultaneously recorded electrogram, picked up from an electrode that was close to the A-V septum on the left side of the heart   This suggests practically continuous electrical activity in the ventricle at the stage of chaotic rhythm   Note that the electrogram does not always settle down to a base line , where the T wave of the electrocardiogram has been interrupted by the succeeding R wave, the new electrogram may begin prematurely, as judged by the fact that the preceding complex does not fall to the level noted with the alternate series of complexes

as a whole and in certain cases at least the termination of the T wave does not represent the passing off of the wave of excitation throughout the entire heart   For example, in the case of a left ventricular premature systole, the right side of the heart is the last part to be excited and the terminal part of the T wave represents the passing off of the wave of excitation from the right side   It is not so easy to explain the interruption of the T waves of a supraventricular complex in this way for then, apart from branch bundle block, the T wave represents the passing off of the wave of excitation on both sides of the heart   Such arguments do not go much further than indicating that we cannot eliminate the possibility that a single cardiac muscle fibre may be capable of responding to a new wave of excitation before the previous wave of excitation has ended

The observations of Moe, Harris, and Wiggers (1942) indicate clearly that a suitable electrical stimulus applied to a ventricle during or just before the descent of the T wave leads to a wave of excitation in the heart muscle, but after such a delay that the resulting R wave came after the termination of the T wave and commonly in the vicinity of the

by the succeeding wave of excitation, an observation that corresponds with the appearance of R waves on T waves but suggests that the phenomenon can take place even within the circumscribed area of the heart from which the electrogram is recorded   It is not unlikely therefore, that cardiac muscle fibres are capable, under certain circumstances, of responding to a new wave of excitation before the previous wave of excitation has ended

EXCITABILITY OF THE MYOCARDIUM AS THE UNDERLYING CAUSE

The data concerning the 17 patients whose cases are reported suggest the probability that " increased excitability " of the myocardium may be an important underlying cause for the appearance of R waves superimposed upon T waves   It is necessary to consider further the meanings of the word excitability as applied to cardiac muscle   Increased excitability has been used in reference to an increased disposition of the cardiac muscle to originate new rhythms   More precisely, however, it should refer to the ease with which the myocardium responds when a stimulus is applied to it   No doubt, under clinical conditions, these two phenomena are difficult to differentiate from each other but evidence suggesting excitability in one sense or another is present in the great majority of cases here quoted   In Cases 1, 2,

* An additional 8 cases, including one with paroxysms of ventricular flutter (electrocardiographic), have been encountered while this paper was in press

TABLE I

Case	Age	Type of Interruption † — S by S	S by V	V by V	Polymorphic Ectopic Vent Complexes	Variability of Interval after antecedent beat	Ectopic Vent Complexes in runs of 2 or more	Variability of Interval between successive beats	Polymorphic Ventricular Complexes of Supraventricular Origin	Types of Rhythm Encountered	Other Electrocardiographic Evidence of Myocardial Damage	Clinical Features	Progress of Patient	Long or short Lengths of Tracing Available
Cardiac Infarction Cases														
1	59	?+		+	+	+	+	+	0	Sinus prem v s	T I isoelectric, T II low or inverted, Intermittent B B Bl	Recent infarction, congestive failure large heart	D S	L
2	46	+		+	+	+	+	+	0	Sinus prem v s, v par tachy	Indefinite	Recent infarction, good clin evidence of infarction	R	S
6	58		+		+	+	0	n a	0	Sinus prem v s	Positive	Recent infarction, good clin evidence of infarction	R	L
9	73		+		0	n a	0	n a	0	Sinus prem v s	Low T I Positive	Recent infarction confirmed P M	D S	S
10	77		+		n a	n a	0	n a	0	Sinus prem v s	T I, T IV inverted Q I deep Positive	Old infarction, angina of effort	D	S
11	79		+		+	+	+	n a	0	Sinus prem v s	Positive	Recent infarction	D	S
"Myocardial Degeneration" Cases														
5	71		+	+	+	+	+	+	0	Sinus aur bigem prem v s	Low T I	Myocard degen	D S	L
7	40		+	+	+	+	+	+	0	Sinus prem v s	Inverted T III	Myocard degen, gallop rhythm, œdema ankles	R	L
8	77		?+		+	+	+	+	+	Sinus prem v s	Isoelectric T I	Myocard degen, art, hyper tension, card asthma	R	L
12	77		+		+	+	+	n a	0	Sinus prem v s prem a s	T III isoelectric	Myocard degen, gallop rhythm	R	L
17	62		+		+	+	0	n a	0	Sinus prem v s	None	Melancholia, circulatory condition discovered incidentally	R	L
Auricular Fibrillation Cases														
3	56	+			n a	n a	n a	n a	+	Sinus par aur fibrillation Aur fibr prem v s	T I, T II low biphasic Aur fibrillation	Thyro-cardiac improved by thyroidectomy	R	S
4	71	+		+	+	+	+	+	+	Aur fibr prem v s	T III low	Confused mental state Im proved in hospital	R	L

TABLE 1—(continued)

										Sinus	Heart block	Large heart	Hypostatic	D	S
11	78	+	+	n a	n a	n a	n a	n a	+	par aur fibrillation heart block	Aur fibrillation	pneumonia			S
14	70	+	+	n a	n a	n a	n a	n a	+	Aur fibrillation	Aur fibrillation, T I, II, III almost isoelectric	Gallop rhythm, Large heart, Great obesity		R	S
15	73	?+	?+	?	n a	+	n a	?	+	Aur fibrillation b b block	Low T I, B B Bl	Congestive failure Emotional shock		R	S
16	66	+	+	n a	n a	n a	n a	n a	+	Par aur fibrillation	Abnormally large P wave	Tachycardia, reasonably fit, otherwise		R	L

† S by S—examples of ventricular complexes of supraventricular origin interrupted by other ventricular complexes of supraventricular origin
S by V—examples of ventricular complexes of supraventricular origin interrupted by ectopic ventricular complexes
V by S—examples of ectopic ventricular complexes interrupted by ventricular complexes of supraventricular origin
V by V—examples of ectopic ventricular complexes interrupted by other ectopic ventricular complexes
n a —not applicable   D S —died suddenly   D —died   R —recovered

4, 5, 7, 8, 9, 12, and 17, it seems probable there is an increased tendency to originate new rhythms Large numbers of premature ventricular systoles arise which, as judged from the shape of the complexés, originate from different foci These ectopic beats occur at a variable time after the preceding beat and it may be thought from this that they probably result from the spontaneous activity of small parts of the cardiac muscle rather than from excitation of the ventricular muscle as the result of " re-entry " of impulses set up during the antecedent systole

In contrast to this we have Cases 3, 13, 14, and 16, with auricular fibrillation and an abnormally rapid beating of the ventricles It may well be thought that the conducting tissue (less probably, ventricular muscle) is responding more readily than usual to the stimuli coming down to it from the auricles

Of the 17 cases, 6 are examples of cardiac infarction In such cases the important pathological change in the myocardium is of comparatively recent origin It is not surprising that in most cases where premature ventricular systoles are the result of a cardiac infarction the ectopic beats appears to arise from many foci Likewise if these premature beats are arising spontaneously as the result of discharge from irritable foci, there is no obvious reason why they should develop at a fixed time after the antecedent normal complex and in fact, in none of the infarction cases here quoted, do we find the premature ventricular systoles at a fixed distance after the antecedent normal beat

In the 6 cases of cardiac infarction described in this paper, R waves are found superimposed on T waves, but in most cases of infarction this phenomenon is not found

R waves superimposed on T waves were found in a miscellaneous group of cardiac cases where there was no cardiac infarction In some of these patients ectopic beats arising in the ventricles are responsible for most of the interrupted complexes These premature ventricular complexes arise from several foci and at variable times after the antecedent complexes It seems probable that there is increased excitability of the ventricular muscle due in these cases to causes other than cardiac infarction In other cases, however, the rhythm has a supraventricular origin In most of such cases the evidence of excitability is two-fold, first the development of an irregular auricular tachycardia due in the present cases to auricular fibrillation and secondly the fact that the ventricles are able to respond to these stimuli by unusually rapid beating

In some patients ectopic rhythms have arisen at one time from the auricles and at another from the ventricles This observation also favours the idea

that the common factor is an increase in myocardial excitability (Cases 4, 5, 12, and 15) Some further evidence is given in the succeeding section

THE SUPERNORMAL PERIOD OF CARDIAC EXCITABILITY

As has been recognized for some time, there is a supernormal period in nerve at the time of the negative after-potential Adrian (1921) showed that a super-normal period could be demonstrated in the ventricle of the frog upon acidifying the fluid in which the tissue was immersed Wastl (1922) demonstrated supernormality in fatigued preparations - Cats anæsthetized with barbiturates invariably showed the supernormal period subsequent to the relative refractory period (Hoff and Nahum, 1938) but decerebrated cats rarely showed such super-normality (Eccles and Hoff, 1934) The super-normal period in the cat's ventricle may coincide with the terminal part of the T wave and when a U wave is present it falls during this stage Wastl (1922) considers that the U wave is in fact the terminal part of the ventricular complex

It is interesting to consider whether any of the examples of R waves upon T waves are distributed in such a manner that the interrupting beats fall chiefly within a phase of super-normality Supernormality might be concerned also in the frequency with which the ventricle is stimulated from auricles in a state of auricular fibrillation If such were the case we would be dealing, presumably, with a super-normality of the conducting tissue Supernormality of the conducting tissue has been postulated by Lewis and Master (1924) and by Goldenberg and Rothberger (1936) Super-normality might be exhibited in relation to premature ventricular systoles and might determine whether a stimulus arising from an irritable focus would be effective and lead to a premature ventricular complex during the supernormal phase of the antecedent heart beat

In the cases described in this paper, most premature beats develop either in the U wave region or on the descent of the T wave In some cases all the premature systoles are confined to these parts of the cardiac cycle An example of this is found in Case 7 At times when this patient was not displaying R waves on T waves the premature beats occurred a little later in the cardiac cycle and mostly in the region of the U wave In some other patients (Case 8) the premature beats could occur during a greater part of the cardiac cycle but were concentrated particularly in the region of the U wave or on the descent of the T wave Similarly, when premature beats interrupted other premature beats or were followed by other premature beats, the

R wave of the second beat occurred very soon after the end of the T wave or during its descent The incidence of the premature beats in these patients could be explained as being largely determined by a super-normal period both in the case of premature beats following normal beats and in premature beats following other premature beats In most patients where interruptions of premature beats by premature beats is observed, examples of the interruptions of normal beats by premature beats are also observed The interruption is not so much determined by the nature of the complexes concerned as by a state of the cardiac muscle Probably, the state of the cardiac muscle that allows the effective generation of these very premature ectopic beats is a state of super-normal excitability of the myocardium It has been stated by Katz (1946) that a super-normal phase does not occur in the normal human heart but may be present in abnormal hearts Scherf and Scholt (1939) also describe a super-normal phase in man The observations reported in this paper are consistent with this view The super-normal phase has been demonstrated in experiments on healthy cats but it has not yet been made clear whether under experimental conditions the heart was exhibiting a phenomenon that would not be obtained under more normal conditions

RELATIONSHIPS OF ELECTRICAL AND MECHANICAL EVENTS WHEN T WAVES ARE INTERRUPTED BY R WAVES

It is not certain that the relationship between electrical and mechanical events in the heart is constant (Katz, 1946) and it may be changed both during health and in disease In a number of our cases in which R waves were encountered on T waves phonocardiograms or alternatively ballistocardiograms were recorded simultaneously with the electrocardiograms In Cases 5 (Fig 5A, B) and 7 it was found that, where the T wave was interrupted by the R wave of the premature systole, the intensity of the first sound produced by the very premature systole was less than that produced by normal heart contractions or by premature contractions that occur later in the cardiac cycle Sometimes the weak first sound was followed by a second sound, in other cases no recorded second sound was observed In those cases where a second sound was associated with a very early premature systole it is realized, with some surprise, that the premature beat must have caused a discharge of blood from the heart and the opening of the semilunar valves must have been sufficient to produce a second sound on closing again Either the antecedent beat had not emptied the ventricles completely or some degree

of filling of the ventricles must have taken place at a time corresponding to the lower third of the descent of the T wave   Other phonocardiograms gave results that were not dissimilar   In Case 5 several ballistocardiograms were taken (Fig 5) and these showed, as expected, that the output from the heart was much less when a premature systole occurred very early in the cardiac cycle, but in all traces taken the ballistocardiographic results suggested that some blood had been discharged into the aorta even during the very premature systoles

THE CLINICAL SIGNIFICANCE OF R WAVES ON T WAVES AND INDICATIONS FOR TREATMENT

A survey of published electrocardiograms shows that R waves on T waves are often seen shortly before the onset of clinical ventricular flutter, also before the onset of experimental ventricular flutter produced in a variety of ways, and in this series R waves on T waves occurred in 6 patients with cardiac infarction of whom 2 died suddenly   These points indicate the possibility that the appearance of R waves on T waves may be of bad prognostic import It would appear that the condition occurs chiefly among cases where there is good evidence of increased cardiac excitability and of substantial myocardial damage   Many of the patients were elderly   Naturally enough where there is already evidence of myocardial disease one may expect a poor prognosis, the question we must ask is whether the finding of an R wave on a T wave, in itself worsens the prognosis in these cases   On this question there is insufficient evidence but nevertheless the distinct indication that the subject deserves further study, first because of the known association, under experimental conditions, between the presence of R waves on T waves and ventricular flutter and fibrillation, secondly because in the clinical material studied there had been instances of sudden death that could be explained reasonably as examples of ventricular flutter or fibrillation The matter is not without practical importance since preliminary observations suggest that the tendency to this particular manifestation can be arrested or greatly diminished by treatment with quinidine, digitalis, or strophanthus, more especially quinidine

Unfortunately the possibility of a useful method of treatment did not emerge at the outset of this investigation, but in two cases of cardiac infarction exhibiting the presence of R waves on T waves the administration of quinidine arrested the premature systoles, and as premature ventricular systoles had been responsible for the interruptions of the antecedent complexes, this phenomenon was thereby eliminated   In the first (Case 6) the patient made an

uninterrupted recovery from the infarction but was readmitted some 3 months later with a second and fatal infarction   On this second occasion there were no premature systoles noted.   In the second (Case 9) the administration of quinidine prevented the premature systoles and eliminated the interruption of complexes   Unfortunately a haematemesis necessitated withdrawal of the quinidine whereupon the premature ventricular complexes recurred   One month after the onset of the infarction the patient was saying how well he felt and he suddenly stopped and was dead in a few seconds   This would appear to be an example of ventricular flutter   In Case 7 the patient was in moderately good condition with little breathlessness and a moderate exercise tolerance, but a gallop rhythm   She was treated with quinidine, this stopped almost all ectopic beats, but unfortunately the drug had to be stopped as she experienced continuous vertigo and headache   On administering strophanthin by intravenous injection the number of premature systoles were much reduced, and those which occurred were found later in the cardiac cycle and after the termination of the T wave   With eight tablets daily of 1/500 grain of strophanthin by mouth, also, the premature systoles were much reduced in number   In view of the increased excitability of the ventricle brought about by substances such as digitalis and strophanthus, 1/200 of a grain of atropine was given thrice daily at the start, this to some extent at least, serves as an anti-fibrillating agent   The patient was much improved and was discharged from hospital

It would seem that the administration of quinidine, digitalis and strophanthin in such cases deserves a trial   Perhaps quinidine is the most likely to prove satisfactory and digitalis and strophanthus are probably potentially dangerous   In any case where cardiac infarction has taken place neither digitalis nor strophanthus should be given unless there is congestive heart failure

SUMMARY

Seventeen cases are described in which R waves appear on the descent of T waves   They appear to be examples of an electrocardiographic syndrome characterized by a group of related abnormalities some of which are explicable in terms of increased myocardial excitability

The presence of an R wave on a T wave indicates that a new wave of excitation starts before the previous wave has ended   It is convenient in these circumstances to speak of a ventricular complex being interrupted before its completion

Ventricular complexes of supraventricular origin may be interrupted by other ventricular complexes

of supraventricular origin or by ectopic ventricular complexes Ectopic ventricular complexes may be interrupted by ventricular complexes of supraventricular origin or by other ectopic ventricular complexes

R waves on T waves may occur with ectopic ventricular systoles, paroxysmal ventricular tachycardia, auricular fibrillation, and auricular paroxysmal tachycardia They may occur in cardiac infarction Theoretically they might occur with ectopic auricular systoles and auricular flutter

When R waves on T waves are due to ectopic ventricular complexes, these are almost always polymorphic and presumably multifocal The ectopic ventricular complexes occur at varying intervals after the antecedent beat and there is a tendency for them to occur in runs of two or three or more beats Even when the presence of R waves is brought about by a supraventricular rhythm (usually auricular fibrillation), polymorphic ventricular complexes are often found

In view of the fact that R waves on T waves are frequent precursors of clinical and experimental ventricular flutter and ventricular fibrillation, it is desirable to consider the significance of this finding for prognosis in man A few of the patients in this series have died suddenly

It is probably advantageous to use quinidine in such patients with multiple premature ventricular systoles This abolished the interruption of T waves by R waves in all of five cases Digitalis and strophanthus also abolish the interruptions in some cases, but have theoretical objections

The significance of this phenomenon in relation to the refractory period of heart muscle, the supernormal phase of cardiac excitability, and the mechanical changes associated with very premature systoles are discussed

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LAY CARDIOLOGISTS

BY

TERENCE EAST

" For so to interpose a little ease " is well enough in these times, even in a scientific journal It is hardly fair to complete the quotation, for the " surmise " of the lay writer is often far from " false "* From time to time, in desultory reading, one's attention is arrested by a good description by a lay author of a clinical condition, those which follow are of cardiovascular interest The description by W N P Barbellion of his disseminated sclerosis in the *Journal of a Disappointed Man* once attracted much interest He also gave an account of his extrasystoles

" Bad heart attack all day Intermittency is very refined torture to one who wants to live very badly Your pump goes ' dot and carry one,' or say, ' misses a stitch,' what time you breathe deep, begin to shake your friend's hand, and make a farewell speech Then it goes on again and you order another pint of beer It is a fractious animal within the cage of my thorax, and I never know when it is going to escape and make off with my precious life between its teeth "

The alarm that these harmless disturbances occasion was also well described by Hugh Walpole in his novel *The Old Ladies*

" A new sound that May had never heard in that house before It was the dripping of a tap   like someone counting time—1, 2, 3, 4, then a pause, then several drips together   May began to count—she counted to ten and after that so many came together that she could count no longer she lay, the sweat on her forehead, her body trembling, her heart running and jumping and missing, and jumping and running She heard it so plainly that it seemed that it must be with her now beside her bed, the running tap "

There are many good clinical references in Kipling's writings The only one of cardiovascular interest is the description in *The Light that Failed* of what would appear to be a patient with aortic regurgitation who has just climbed a flight of stairs,

* ' For so to interpose a little ease let our frail hearts dally with false surmise "—Milton's *Lycidas*

" His lips were parted and pale, and there were deep pouches under the eyes   ' Weak heart,' said Dick to himself as he shook hands, ' very weak heart. His pulse is shaking his fingers ' "

Samuel Johnson diagnosed the cardiac origin of his asthma correctly Writing to Dr Brocklesby, his physician, after a visit to Lichfield, he remarked, " The asthma has no abatement Opiates stop the fit, so that I can sit and sometimes be easy, but they do not procure me the power of motion I am looking into Floyer, who lived with his asthma to almost his ninetieth year His book by want of order is obscure, and his asthma not of the same kind with mine " Later in the year he died of heart failure, and the autopsy showed that he had had high blood pressure His well-known account of his stroke which he had had the year before agrees with this.

" I went to bed, and in a short time waked and sat up, as has long been my custom, when I felt a confusion and indistinctness in my head, which lasted, I suppose, about half a minute I was alarmed, and prayed God, that however he might afflict my body, he would spare my understanding   I had no pain, and so little dejection in this dreadful state, that I wondered at my own apathy, and considered that perhaps death itself, when it should come, would excite less horror than seems now to attend it

" In order to rouse the vocal organs, I took two drams Wine has been celebrated for the production of eloquence I put myself into violent motion, and I think repeated it, but all was in vain I then went to bed, and strange as it may seem, I think slept When I saw light, it was time to contrive what I should do Though God stopped my speech, he left me my hand, I enjoyed a mercy which was not granted to my dear friend Lawrence, who now perhaps overlooks me as I am writing, and rejoices that I have what he wanted My first note was necessarily to my servant, who came in talking, and could not immediately comprehend why he should read what I put into his hands

' " I then wrote a card to Mr Allen, that I might have a discreet friend at hand, to act as occasion

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should require   In penning this note, I had some difficulty, my hand, I knew not how or why, made wrong letters   I then wrote to Dr Taylor to come to me, and bring Dr Heberden   and I sent to Dr Brocklesby, who is my neighbour   My physicians are very friendly, and give me great hopes, but you may imagine my situation   I have so far recovered my vocal powers, as to repeat the Lord's Prayer with no very imperfect articulation"'

He made rapid recovery, and had " leave to wash the cantharides " from his head a fortnight after the stroke, which was no doubt hypertensive encephalopathy

In *Treasure Island* there is a short vivid description of an apoplectic attack   " I heard a loud fall in the parlour, and running in, beheld the Captain lying full length on the floor   He was breathing very loud and hard, but his eyes were closed, and his face a horrible colour "

Whether the philosopher Seneca * really had angina pectoris is doubtful   He described an attack in these words (*Epistulæ Morales LIX*) " But I have been assigned, so to speak, to one special ailment   The attack is of very brief duration, like that of a squall at sea, it usually ends within an hour   I have passed through all the ills and dangers of the flesh, but nothing seems to me more troublesome than this   And naturally so, for anything else may be called illness, but this is a sort of continued ' last gasp '   Hence physicians call it ' practising how to die ' "   As he lived long after and died by his own hand ultimately, perhaps his _" meditatio mortis " was really bronchial asthma In the *Swan of Litchfield* by J E Pearson, there is an excellent account of angina of effort, which culminated in a fatal attack on stooping   Anne Seward, the heroine of the book, describes the death of her old friend Mr Saville, which took place on August 16, 1803

" In April he began to complain, at times, of a stricture in his breast—a slight pain there, and a difficulty in breathing on going upstairs, or uphill A disorder so entirely new to his frame startled me, but neither of us supposed the symptoms dangerous His appetite, his spirits good, and the malady apparently trivial and infrequent, yet alas!   I am now convinced these were the presage of the disease which destroyed him "   He had been dressing for a party   " Soon after he cut a corn, which pained him, and in that operation had been stooping over his stomach some time, when suddenly a tremendous seizure of the late kind attacked him, and in a quarter of an hour struck him from the land of the living "

* Translation by-R M Gummere (Loeb series)

The following passage from *Middlemarch* describes what might well have been a painless attack of myocardial infarction

" Dorothea had not looked away from her own table when she heard the loud bang of a book on the floor, and turning quickly saw Mr Casaubon on the library steps clinging forward as if he were in some bodily distress   She started up and bounded towards him in an instant, he was evidently in great straits for breath   Jumping on a stool she got close to his elbow and said with her whole soul melted into tender alarm —' Can you lean on me, dear?'   He was still for two or three minutes which seemed endless to her—unable to speak or move, gasping for breath   When he at last descended the three steps and fell backwards into the large chair, he no longer gasped, but seemed helpless and about to faint "

His physician, Mr Lydgate, makes his diagnosis and prognosis   "My conclusions are doubly uncertain, uncertain not only because of my fallibility, but because diseases of the heart are eminently difficult to found predictions on   I believe you are suffering from what is called fatty degeneration of the heart which was first divined and explored by Lænnec   It is my duty to tell you that death from this disease is often sudden   At the same time, no such result can be predicted   Your condition may be consistent with a tolerably comfortable life for another fifteen years or even more "

Mr Casaubon was found dead sitting in his summer house, not long after this   The prognosis which George Eliot puts into the mouth of the doctor is cleverly worded, and would be a model of instruction for a student

An atypical attack of coronary occlusion seems to be the subject of one of Cowper's letters (May 1785)

" Mr Ashburner, the elder, went to London on Tuesday sennight in perfect health and in high spirits, so as to be remarkably cheerful, and was brought home in a hearse the Friday following Soon after his arrival in town, he complained of an acute pain in his elbow, another in his shoulder, then in both shoulders, was blooded, took his doses of such medicine as an apothecary thought might do him good, and died on Thursday morning at ten o'clock.   It is not common, however, for men at the age of thirty-six to die so suddenly," he comments, in those days, too, early cases appear to have occurred, one may remark.

In Horace Walpole's letters there are many medical references, chiefly on the subject of gout. There is one which may be included here   In one he laments the death of his friend Mr Chute, also a victim of gout, in a letter to Sir Horace Mann in Florence

" I was never alarmed till last summer when he had a low lingering fever and sickness, and pain in his breast with returns of the recurrent palpitation   On Thursday last   I was told he was very ill, I found him in bed, he had so violent pain in his breast that two days before he had sent for Dr Thomas, who had given him one hundred drops of laudanum and asafœtida   Mr Chute said ' It is not gout, I have had my palpitation and fear it is something of a polypus' ' "

He died suddenly   Walpole comments " It certainly was a polypus, his side grew immediately as black as ink "   If this account is correct it might possibly have been a dissecting aneurysm, with rupture into the pleura.

To turn to more modern writers, there is a first-rate account of the symptoms of cardiac infarction in *Time Must Stop* by Aldous Huxley   -

' And then suddenly the pain was like a red hot poker thro' his chest   He felt dizzy and a whirling blackness obscured the outside world He lowered himself unsteadily onto the seat and almost immediately felt a good deal better Just as his arm was at full stretch the pain returned— but in a new form   for now it had become, in some indescribable way, obscene as well as agonizing And all at once he found himself panting for breath, and in the clutch of a new terror more intense than any he had ever experienced before   Then all at once the pain shot down his left arm, nauseating, disgusting, like being hit in the wind "

Sparkenbroke by Charles Morgan provides another good description of an attack of angina brought on by cold

" In the evening, a little before dusk, while he was washing in cold water, he received warning that a paroxysm was about to seize him   A stiffness of neck and shoulder was followed by a deep aching within the left arm, and, after a little interval, by an agony within the leg as though a wedge were being driven into the bone's marrow and the bone itself split   He had dragged himself from the washstand to his bed and covered himself, for he was half naked, his body still wet and now bitterly cold As the pain increased, the leg stiffened, his back arched, his arm, beyond his will, was twisted under his back, and he cried out, for his ampoules of amyl nitrite were in the coat he had taken off   Bissett, hastening in, put one of these into a handkerchief and the handkerchief within the grip of his hand He crushed it and inhaled   For a little while it gave relief   His body was loosened from its contortion and he lay against pillows, struggling for breath, asking that he might escape the greater paroxysm of the body itself   -

" But the agony swept upon him afresh   There appeared in his mind an image of his chest as a bony shell within which the organs of his body were being compressed by cords   The organs themselves had individuality and voices, he heard them cry out, saw them twist and spurt, emptying their blood-red to a pearly and sweating grey   Far off, within the divisions of his fingers, were folds of linen, he raised them up, a handkerchief was twined against his nostrils, which sucked in its fumes   They had the smell of comfort, but a gust of torment swept them away, and he saw Bissett laying hot compresses on the bony shell, which heat could not penetrate He gathered his knuckles into the softness of his throat." *

The art of writing clinical descriptions is almost lost nowadays   The dry deserts of modern medical literature would make better reading if something of the charm of these lay authors could be imparted to them'

* Some of these excerpts, with others less pertinent to cardiology have appeared in the *King's College Hospital Gazette* (1947), Vol 26

EDITORIAL NOTE

What was almost certainly a paroxysm of auricular fibrillation has been described in the literature of the 1914–18 war, when the author was almost exhausted by the hardships involved in escaping on foot from a prisoner's camp   " Owing to the mud I began to feel frightfully tired   I staggered, and quite suddenly I collapsed and lay on the ground unable to move.   I managed to put my hand over my heart and could feel that it was running most irregularly and misfiring in an extraordinary way   After about a quarter of an hour it got much better, so I had a few mouthfuls of bread and went on again "   (*The Escaping Club*, by A J Evans   John Lane, Lond , 1929, p 224)   The sudden collapse and the sudden recovery make it much more likely that this was paroxysmal fibrillation than a bout of frequent extrasystoles

East has included cardiovascular disease and this allows a reference to the cardiovascular accidents that give more play to the lay writer because their results are more obvious in disorders of behaviour and mannerisms   Charles Dickens has many such

instances and shows by these, as in other ways, his great powers of accurate observation. The mental changes and -change of temperament in Mrs Gargery in *Great Expectations* after a blow on the back of the head, and the detailed account of the degenerative changes following on cerebral arteriosclerosis on the Honourable Mrs Skewton, the mother of *Mrs Dombey*, are detailed and accurate and must have been based on personal observation of cases. These have been dealt with fully by Russell Brain in the *London Hospital Gazette*, January 1942. He is able to diagnose that Mrs Gargery had a severe contusion of the left temporoparietal region causing jargon aphasia and word deafness and some traumatic dementia, with injury to the third or sixth cranial nerve leading to diplopia.

An equally detailed diagnosis of a hæmorrhage from a posterior inferior cerebellar artery in the case of James Armitage, alias Trevor (*The Gloria Scott*) could be made from the pages of *Conan Doyle*, but perhaps this is an unfair addition as medical authors have been excluded. Even so, readers who look for it may be surprised by the amount of accurate medical detail in the Sherlock Holmes stories. Major Sholto died from left ventricular failure, and orthopnœa is rightly emphasized as a leading symptom. " When we entered his room he was propped up with pillows and breathing heavily

grasping our hands he made a remarkable statement in a voice broken as much by emotion as by pain. At this instant a-horrible change came over his expression—his eyes stared wildly, his jaw dropped, and he yelled, ' Keep him out.' We rushed to the window and when we returned his head had dropped and his pulse ceased to beat " (*The Sign of Four*). No wonder his son, Thaddeus Sholto, became hypochondriacal about his mitral valve.

The other is a good description of an aortic aneurysm. When Jefferson Hope was arrested he remarked that he might not live for the trial. " It isn't suicide I am thinking of, put your hand on my chest," he said. Watson did so and at once became conscious of an extraordinary throbbing and commotion inside. The walls of his chest seemed to quiver as a frail building would when some powerful engine was at work. In the silence of the room he could hear a dull humming and buzzing noise which proceeded from the same source. Watson diagnosed an aortic aneurysm and the diagnosis was confirmed by his death from its rupture that after noon (*The Study in Scarlet*).

I have dealt more fully with these medical aspects in the *Guy's Hospital Gazette* (Vol 48, p 524, 1934 and Vol 49, p 2 and 27, 1935).

MAURICE CAMPBELL

THE DURATION OF NORMAL HEART SOUNDS

BY

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The gradually increasing importance of phonocardiography creates problems that at times are difficult to solve—among them, that of deciding whether the complexes revealed by a tracing are still within normal limits   Therefore, knowledge of exact normal data is of interest as a basis for the study of clinical tracings

Many authors studied the normal heart sounds between 1907 and 1937   Their data have been reviewed and can be found in a comprehensive work by Rappaport and Sprague (1942)   As, however, those studies were made by means of various techniques, any comparison with our data is impossible and their detailed quotation needless

The only article that dealt with the same problem and used a similar technique is by Rappaport and Sprague (1942)   Our study was made by means of the stethoscopic microphone, therefore, reference will be made only to data obtained by those authors using this microphone

Rappaport and Sprague studied 33 normal persons between the ages of 19 and 38, and gave the maximal and minimal duration of the heart sounds recorded at the apex (Table I)   No average data were given by them

While these data are extremely useful, they are not sufficient for clinical studies because (a) they refer to only one age group, (b) they give only the total duration without breaking down the sounds into their various phases, and (c) no average figures are given   For these reasons, an additional, more comprehensive study was considered necessary

THE MAIN PHASES OF THE CARDIAC SOUNDS

As known, the first and second sounds are actually " noises," consisting of various vibrations having different frequencies   Both the first and the second sounds are caused by four different factors   Four different components were, therefore, described in both the first (Orias and Braun Menendez, 1939) and second sounds   (Rappaport and Sprague, 1941 and 1942)

The systematic clinical use of phonocardiography convinced one of us (Luisada) of the extreme variability of the complexes of the heart sounds even in normal subjects   In many of these, separation of the complexes into four components is impossible   On the other hand, the occasional observation of cases where the large vibrations of either the first or the second sound are far more numerous than in the average tracing forces one to know not only the overall duration of the sounds but also the duration of their individual components   For this reason, while we fully recognize the accuracy

TABLE I

DATA OF RAPPAPORT AND SPRAGUE

	First sound (sec)	Second sound (sec)	Third sound (sec)	Interval II–III (sec)
Maximum duration	0 165	0 145	0 085	0 240
Minimum duration	0 105	0 085	0 030	0 160

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and the theoretical importance of dividing the sound complexes into many components, we think that a simplified system of study may have practical value The following description is based on purely practical considerations

In both the first and second sounds, the main part of the complex consists of large irregular vibrations, caused in the main by valvular events, while the beginning and the end of the sound is formed by slower vibrations Therefore, division of each sound into three phases is relatively easy (Fig 1)

Tables II and III show the causes of these phases and correlate them with the various components of each sound

As will be noted, our division into components of the first sound is slightly different from that of Orias and Braun Menendez (1939) for the following reasons

(*a*) The muscular factor gives vibrations that may be superimposed on all the others   On the other hand, a slow vibration frequently initiates the first sound in cases of complete A-V block or auricular fibrillation   This is due to the isometric contraction of the ventricles   It is difficult to say whether the heart muscle itself is causing it or whether it is due to initial vibrations of the mitral and tricuspid valves preceding their closure

(*b*) The valvular factor gives vibrations that
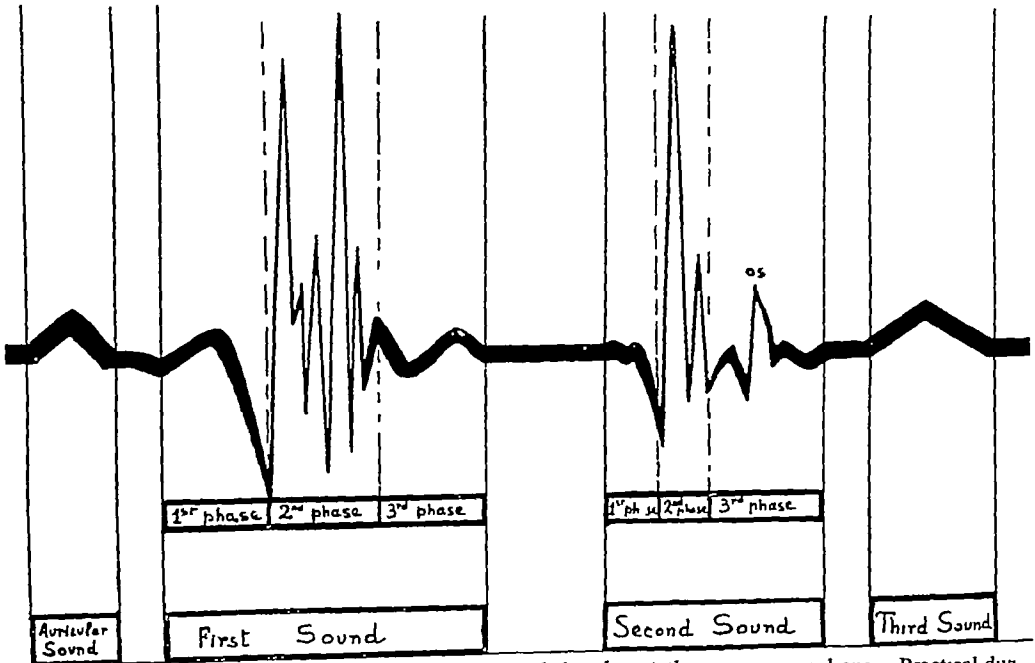
FIG 1 —Diagram of a normal phonocardiogram recorded with a stethoscopic microphone   Practical division of the first and second sounds into three main phases

TABLE II

CAUSAL AND PRACTICAL DIVISION OF THE FIRST SOUND COMPLEX

Component	Cause	Type of vibration	Phase (new terminology)
1st	Auricular residual vibrations	Coarse / Small	1st phase, or phase of the coarse, initial vibrations
2nd	Vibrations due to the isometric contraction of the ventricles	Coarse / Small	
3rd	Vibrations due to the closure of the A-V valves	Fine / Large	2nd phase, or phase of the fine, large vibrations
4th	Vibrations due to the opening of the semilunar valves	Fine / Large	
5th	Vibrations due to the ejection of blood and to arterial distention	Coarse / Small	3rd phase or phase of the coarse, final vibrations

TABLE III

CAUSAL AND PRACTICAL DIVISION OF THE SECOND SOUND COMPLEX

Component	Cause	Type of vibrations	Phase (new terminology)
1st	Vibrations preceding the closing of the semilunar valves	Coarse / Small	1st phase, or phase of the coarse, initial vibrations
2nd	Vibrations caused by the closure of the semilunar valves	Fine / Large	2nd phase, or phase of the fine, large vibrations
3rd	Arterial vibrations	Fine or coarse / Small	
4th	Vibrations due to the opening of the A-V valves	May be fine / Usually coarse and small	3rd phase, or phase of the terminal vibrations

often are clearly separated (Fig 2 and 3) and may even cause an audible splitting of the sound   Both A-V valve closure and semilunar valve opening are accompanied by rapid large vibrations   The latter are clearly separated from the following vibrations of vascular origin

On the contrary, the theoretical division of the second sound into four components, as made by Rappaport and Sprague, is exact and should not be changed   It should be pointed out, however, that the vibration due to the opening of the mitral valve may become audible even in normal subjects and give a high wave on the tracings, as reported by one of us (Luisada, 1943 and 1948) and shown by Fig 4

RESULTS OF THE STUDY

Our study was based on the private collection of one of us (Luisada), consisting of over 1500 phonocardiograms   Cases with a clinical diagnosis of heart disease, an abnormal electrocardiogram, or a recorded murmur were excluded   This left 185 cases which, grouped by age, were divided as follows

(a) 4 cases of foetal sounds recorded during various stages of pregnancy

(b) 1 case below 4 years of age

(c) 2 cases between 4 and 10 years of age

(d) 7 cases between 11 and 20 years of age

(e) 56 cases between 21 and 40 years of age

(f) 38 cases between 41 and 60 years of age

(g) 17 cases above 60 years of age
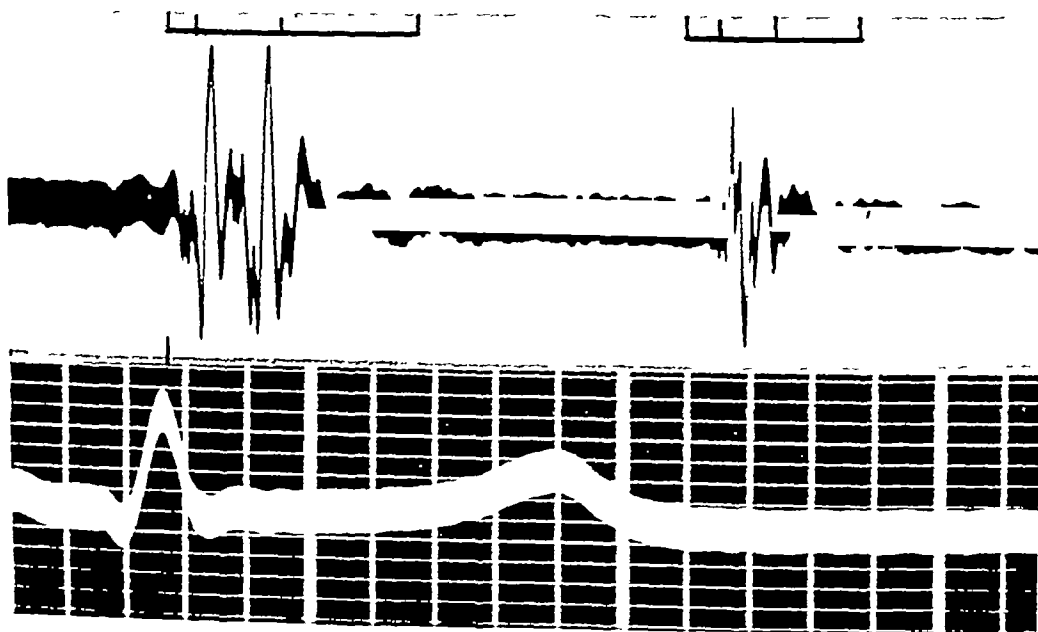
FIG 2 —Phonocardiogram of a normal subject, aged 24 years   The first sound presents two higher vibrations in phase 2

On account of the small number below 10 years of age, the average figures were made only for those above that age In each case, the study was made on phonocardiograms recorded by means of a Stetho-cardiette and a stethoscopic microphone with a large funnel *, only tracings recorded at the apex (181 cases) and at the aortic area (73 cases) were considered (fœtal sounds excepted)

The data that were measured were as follows

(1) Duration of the auricular sound from beginning to end

(2) Total duration of the first sound, from the beginning of the coarse initial deflection to the end of the last coarse vibration of vascular origin †

(3) Partial durations of the three phases of the first sound (coarse initial vibrations, high and fine central vibrations, and coarse final vibrations)

(4) Total duration of the second sound, from the beginning of the coarse, initial vibrations to the end of the coarse final vibrations

(5) Partial duration of the three phases of the second sound (coarse initial vibrations, high and fine central vibrations, and coarse final vibrations including the opening sound of the mitral valve)

(6) Interval between the beginning of the auricular sound and the beginning of the first sound (a–I)
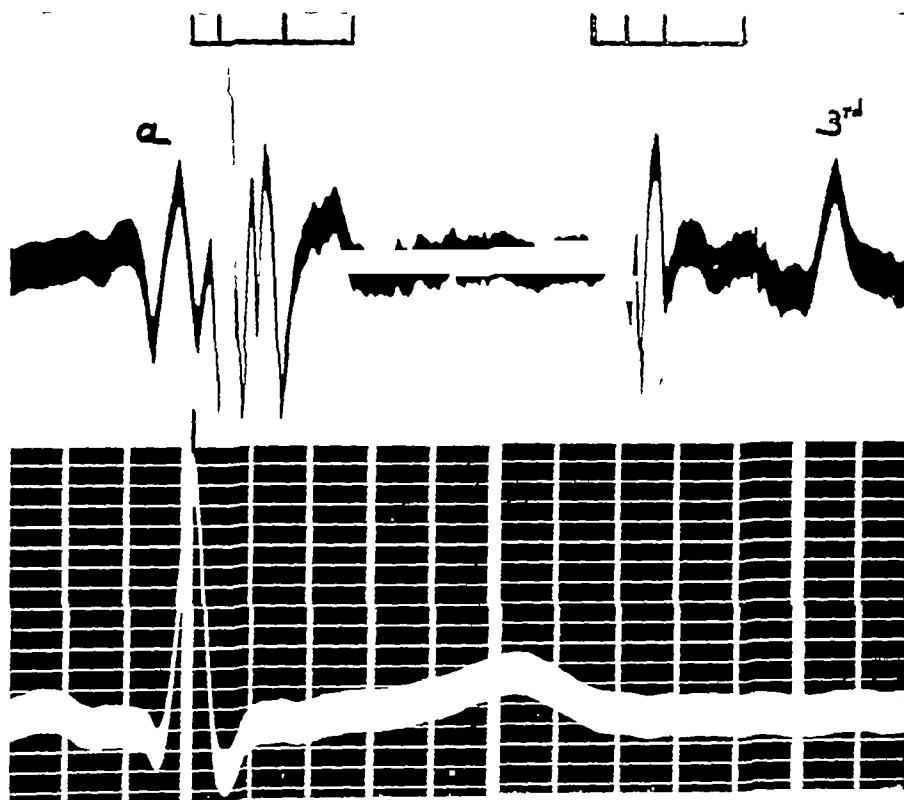
Fig 3 —Phonocardiogram of a boy of 15 years   Loud auricular sound very close to the first sound, third sound   In this case, an arbitrary setting of the beginning of the first sound at the peak of R wave of the electrocardiogram would have been necessary as no clear cut division exists between auricular and first sounds

* In the adults, a funnel having 5 cm of diameter was used in children, a smaller funnel having a diameter of 3 7 cm was preferred

† In a few cases, it was noted that the auricular sound gave vibrations lasting up to the beginning of the phase of large vibrations of the first sound   In others, no vibration of a coarse type preceded this phase In order to obtain a clear-cut point in such cases, the peak of the R wave of the electrocardiogram was taken as the initiation of the first sound as an arbitrary and practical reference which may entail a slight error
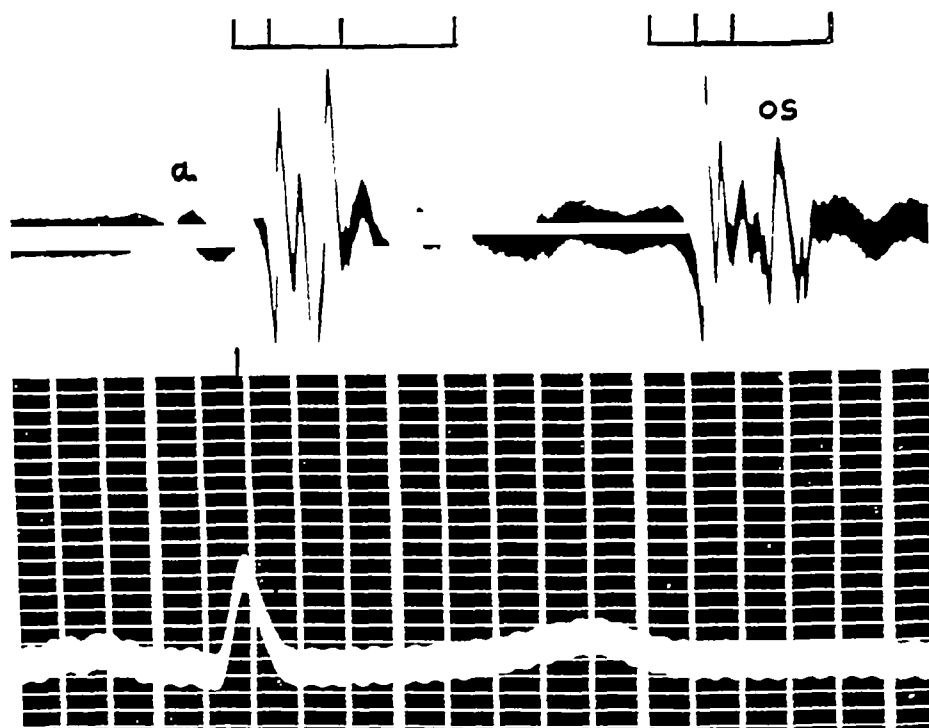
FIG 4 —Phonocardiogram of a normal woman of 33 years   Two higher vibrations are present
in phase 2 of the first sound   The second sound includes a high vibration (os) at the
opening of the mitral valve
   The subject has been followed for eight years since this tracing and repeated phono-
cardiograms recorded.   No heart disease was ever recognized   Subsequent tracings in-
dicated a more conventional aspect of the second sound

(7) Interval between the peak of the largest oscillation of the second sound and the beginning of the third sound (II–III)

The results of the study are reported in the following tables   Occasional small differences occur between the average figure of the total duration of the first or second sound and the average sum of the three phases of each   This is due to the fact that the first phase was measured only in a percentage of cases (indicated in parenthesis) while in others, with no visible vibration occurring in that phase, no measurement was possible

A summary of the protocols of our observations is given here   Table IV shows the average duration of the heart sounds and their phases and Table V indicates the extreme variations of these sounds

The average length of the first sound above the age of 10 was found to be 0 146 sec at the apex and 0 140 sec at the aortic area

The average length of the second sound in the same conditions was found to be 0 097 and 0 104 sec ,

respectively   That of the third sound was found to be 0 059 and 0 042 sec

The average interval separating the beginning of the auricular sound from that of the first sound was found to be 0 058 sec for both areas, while that separating the main oscillation of the second sound from the beginning of the third, 0 15 sec at the apex and 0 17 sec at the aortic area *

The extreme variations of the first and second sounds are indicated in Table V   Between the ages of 11 and 20, the first sound varied from 0 12 to 0 16 sec at the apex and from 0 11 to 0 16 at the aortic area, and the second sound, from 0 08 to 0 18 sec at both areas

Between the ages of 41 and 60, the first sound varied from 0 07 to 0 22 sec at the apex and from 0 09 to 0 22 sec at the aortic area, and the second sound, from 0 05 to 0 16 and from 0 06 to 0 14 sec , respectively

* The latter figure was obtained on a small percentage of the cases (9 per cent)

TABLE IV

AVERAGE DURATION OF THE HEART SOUNDS, THEIR PHASES AND THEIR INTERVALS *

Age groups (years)	First Sound (sec)				Second sound (sec)				III sound (sec)	a–I (sec)	II–III (sec)
	Total	1st phase	2nd phase	3rd phase	Total	1st phase	2nd phase	3rd phase			
Fœtal sounds	0 085	0 010	0 025	0 055	0 055	0 010	0 027	0 020	—	—	—
Below 4	0 070	—	0 040	0 030	0 060	—	0 020	0 040	—	—	—
4–10	0 120	—	0 040	0 080	0 065	—	0 015	0 050	0·050	0 060	0 12
	0 145	0 020	0 070	0 065	0 110	0 010	0 055	0 050	0 040	0 060	0 14
11–20	0 147	0 016	0 069	0 071	0 097	0 018	0 015	0 056	0 050	0 060	0 14
	0 147	0 010	0 064	0 066	0 120	0 020	0 034	0 056	—	0 055	—
21–40	0 146	0 020	0 063	0 078	0 107	0·020	0 028	0 069	0 061	0 064	0 16
	0 145	0 020	0 060	0 071	0 114	0 018	0 043	0 055	0 043	0 072	0 18
41–60	0 149	0 020	0 057	0 080	0 097	0 016	0 024	0 068	0 057	0 061	0 18
	0 144	0 020	0 064	0 068	0 098	0 013	0 040	0 053	0 040	0 052	0 19
Above 60	0 141	0 024	0 050	0 080	0 087	0 020	0 025	0 053	—	0·050	—
	0 123	0 023	0 063	0·054	0 085	0 010	0 038	0 044	—	0 060	—
Overall averages for ages above 10 years	0 146	0 020 (46%)	0 060	0 077	0 097	0 018 (46%)	0 023	0 061	0 059 (50%)	0 058 (78%)	0 15 (50%)
	0 140	0 020 (55%)	0 063	0 065	0 104	0 015 (38%)	0 039	0 052	0 042 (9%)	0 058 (45%)	0 17 (9%)
	—		—	—	—		—	—			

* NOTE The top figures refer to measurements at the apex, the figures below are those from the aortic area

TABLE V

EXTREME VARIATIONS OF THE HEART SOUNDS AND THEIR MAIN PHASES

Ages	First sound				Second sound			
	Maximum (sec)		Minimum (sec)		Maximum (sec)		Minimum (sec)	
	Total duration	2nd Phase	Total duration	2nd phase	Total duration	2nd Phase	Total duration	2nd phase
				APEX				
11–20	0 16	0 12	0 12	0 04	0 12	0 04	0 08	0 01
21–40	0 22	0 10	0 09	0 02	0 18	0 08	0 04	0 01
41–60	0 22	0 10	0 07	0 03	0 16	0 05	0 05	0 01
				AORTIC ARFA				
11–20	0 16	0 08	0 11	0 06	0 12	0 04	0 08	0·03
21–40	0 22	0 10	0 10	0 03	0 16	0 10	0 08	0·03
41–60	0 20	0 09	0 09	0 04	0 14	0 06	0 06	0·02

At the apex, the maximum duration of the second phase, that of the large oscillations, was found to be 0 12 sec for the first sound and 0 04 sec for the second sound in the younger age group, 0 10 and 0 08 sec, respectively, for the group between 21 and 40, and 0 10 and 0 05 sec for the older age group At the aortic area, these same oscillations measured 0 08 and 0·04 sec for the first group, 0 10 sec for both sounds, for the second age group, and 0 09 and 0·06, for the group between 41 and 60

On the other hand, the *average duration* of this phase was found to be 0 06 sec for the first sound and 0 023 sec for the second, at the apex, and 0 063 and 0 039 sec, respectively, at the aortic area

DISCUSSION

A comparison of our data with those of Rappaport and Sprague (1941, 1942) shows that our figures were found to be longer for both sounds and also for maxima and minima This may be explained partly by the larger number of subjects studied and partly by the different way of measuring the sounds which, in our case, is illustrated by Fig 1

We believe that breaking the sounds into three phases provides an easier and more rapid method of determining the length of the most important phase, that of large oscillations, which are chiefly connected with valvular events of the heart *

As a study of the protocols will show, a total duration of the sounds (chiefly of the first sound) that far exceeds the average is found in only a few stray cases This total duration is increased because

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* Whenever an accurate break-down of the sounds into their components is necessary because the phonocardiogram is used as a time reference for other tracings (cardiogram, phlebogram, pneumocardiogram, or fluorocardiogram), the division should follow the lines previously indicated by Orias and Braun Menendez and by Rappaport and Sprague with the slight modification indicated in Table II for the first sound complex

the third phase, mainly due to coarse vascular vibrations, is longer than average This observation increases the importance of separately measuring the three phases of each sound

SUMMARY AND CONCLUSIONS

The authors have studied the duration of the heart sounds and their intervals in a series of phonocardiograms recorded in 185 normal subjects, making use of a stethoscopic microphone

The difficulty in the measurement of the normal heart sounds led the authors to propose a new practical division of these in the phonocardiogram for general clinical work Both the first and the second sounds are divided into three phases—the first phase of small and slow vibrations, the second of high and rapid vibrations, and the third of small and slow vibrations

A sound should be considered abnormal not only when its total duration is prolonged but also when the duration of the phase of large vibrations is beyond the maximum normal duration of that phase

For each of the various age groups, total duration and partial durations of the sounds were measured by the authors Maximum and minimum and average figures are given The intervals between auricular sound and first sound, and those between the second and third sounds are also studied in the various age groups

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A LOUD-SPEAKER STETHOSCOPE FOR CLINICAL TEACHING

BY

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An equipment was required that would enable a number of students to listen simultaneously in auscultation of a patient's chest The method adopted is to pick up the sounds by means of a microphone held on the chest, amplify them electrically, and reproduce them at a loud-speaker The problem differs from that of phonocardiography in two main respects first, the subjective effect on the listener must be as similar as possible to auscultation with a stethoscope, which means that certain *components of the sounds, too small to affect the* phonocardiograph record, must be faithfully reproduced, and at the same time frequencies that are not well picked up by a stethoscope must be correspondingly attenuated by the electrical system, and secondly, oscillation (" howling ") is liable to occur *due to the microphone picking up the air-borne* sound from the loud-speaker

There is also a fundamental difficulty The relative sensitivity of the human ear to different frequencies depends on the amplitude of the sound, so that if, by one setting of the amplifier, a student at a certain *distance from the loud-speaker* hears exactly what he would hear with a particular stethoscope, another at a different distance will not get the same subjective effect If a high standard of fidelity is demanded, this fact probably limits the method to fairly small groups

Again, students at a *little distance from the* patient are at a disadvantage with regard to discrimination, conscious or subconscious, against sounds due to accidental movements of the chestpiece on the skin, and to discrimination against breath sounds when *listening to heart sounds and murmurs,* because they cannot see small movements Thus it might be that the best results would be obtained by a compromise that sacrificed fidelity slightly in order to reduce the relative amplitude of such sounds

Finally *there are technical difficulties due to the* very low frequencies of the *important sounds, which* go below the range of a¹l but the best commercial acoustic equipment, and due to the great range of amplitude from the large very low-frequency components of the first heart-sound to the smallest audible *murmur*

In the equipment described in this paper, the main difficulties have been overcome, and satisfactory reproduction is believed to have been achieved for at least twenty students at a time No actual teaching has been done with the equipment at the time of writing The total cost, apart from time, was about £70

DISCUSSION OF THE PROBLEM IN THE LIGHT OF PREVIOUS WORK

The equipment is required to pick up from the chest normal and pathological cardiac and respiratory sounds, and to reproduce them by a loud speaker to give as nearly as possible the same effect as auscultation with a stethoscope Extraneous sounds, such as those due to *friction on the skin and* air-borne sounds of all kinds, are not required and should be reproduced as little as possible consistent with the main requirement For the design of the equipment, therefore, information is required on the *frequency response of stethoscopes and on the range* of frequency covered by the wanted sounds The equipment should be designed so that the frequency response is the same as that of a stethoscope over this wanted range of frequency, and *outside this range the less the response the better*

Cabot and Dodge (1925) studied the frequency distribution of heart and breath sounds, mainly pathological, over the range 30 to 2600 c/s, by a method that is directly applicable to the present problem *They switched different filters in turn into* their amplifier and listened for any change in the quality of the sounds as reproduced by it *They*

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found that all components of heart sounds and murmurs were below 1000 c/s, and most were below 660 c/s The lower limit was in some cases 120 c/s, but in others there were components down to the lower limit of their apparatus Breath sounds were almost entirely within the range 120 to 1000 c/s At the date of their work the electrical equipment can hardly have been good enough to give a high standard of fidelity Brooker (1946), who describes the equipment used in making gramophone recordings for Stokes (1946), found that although most of the energy in the sounds was below 1500 c/s, an amplifier that cut off above 2000 c/s did not give perfect reproduction, and he used one which went up to 4500 c/s in spite of the accompanying disadvantage of increased background noise The lower limit of his amplifier was 30 c/s, but he believed that lower frequencies were present and influenced the total subjective effect

Mannheimer (1940) has analysed heart sounds and murmurs in normal children and children with congenital heart disease He used amplifiers incorporating combinations of good filters with measured characteristics, covering a number of frequency bands, the lowest being 0 to 100 c/s and the highest 500 to 1000 c/s In different cases he found components both of normal sounds and of murmurs in all his frequency bands His apparatus (which was primarily for phonocardiography) cut off all components above 1000 c/s, and this he found advantageous in reducing the effect of air-borne disturbances

The absolute measurement of the frequency response of a stethoscope is difficult In the conditions in which it is used, the frequency response depends not only on the design of the instrument itself, but also on the degree of acoustic mis-matching both where the sound is transferred from the patient's body to the chest-piece and where it is transferred from the ear-pieces to the physician's ears, and unless special precautions are taken the degree of mis-matching at one or both places will be different under the conditions of the experiment from that under practical working conditions It is of course also necessary to know and correct for the frequency response of the source of sound (e g a loud-speaker), and of the microphone and other apparatus used for measuring the amplitude transmitted by the stethoscope No account has been found of a measurement of this kind in which a full technical description of the apparatus has been given, and it seems likely that authors have failed to realize the importance of reproducing exactly the acoustical mis match which occurs in practice A technique in which these matters are fully taken account of, is described in a Medical Research Council Special

Report (1947), and was used for measuring the performance of hearing aids Some such technique could be applied to measurement of the frequency response of a stethoscope, but as far as I know this has not been done

Rappaport and Sprague (1941) have attempted to measure the frequency response of stethoscopes and give a theoretical response curve for an amplifying stethoscope which should reproduce the effect of " a theoretically average acoustical stethoscope," but it does not seem that their technique was adequate for the reasons just discussed Their curve falls off steadily from 200 c/s downwards, to −20db at 30 c/s

Comparison of the effects of different stethoscope chest-pieces is not so difficult By putting a source of sound in the heart of a cadaver and applying the different chest-pieces to the chest, Johnstone and Kline (1940) closely simulated the conditions of clinical use as far as the acoustical mis-match at that end was concerned They compared different stethoscopes over the range 20 to 800 c/s, and from their curves it appears that the main effect of a diaphragm, compared with an open bell, is to attenuate the lower frequencies and so increase the relative high-frequency response

Many whole loud-speaker equipments for teaching are mentioned in papers from 1920 onwards, but usually without precise information about frequency response Gamble and Replogle (1924) describe the apparatus used by Cabot (1923), and Gamble (1924) describes improvements to the apparatus and the results of experience after a few months' use Their trials with loud-speaker reproduction were unsatisfactory, and they used a telephone type of output device to which an ordinary stethoscope was applied They found that a filter cutting off sounds above 660 c/s gave the best results for routine use, and that additional filters were useful for accentuating particular sounds and murmurs, in particular one passing frequencies below 140 c/s and one passing frequencies above 130 c/s Rappaport and Sprague (1941) discuss the reasons for poor results with loud-speaker equipments, and emphasize the importance of adequate loud-speaker power-handling capacity and freedom from resonances, as well as correct frequency response of the whole equipment The advantages of loud-speaker reproduction for teaching purposes are discussed by Henriques (1937)

As regards choice of microphone, since the introduction of the piezo-electric crystal microphone this has been unanimously accepted as the best type for the purpose (e g by Sacks and Marquis (1935) and Rentschler (1936), etc) My own experiments with a few other types which happened to be available agree with this

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CHARACTERISTICS REQUIRED FOR THE EQUIPMENT

The simplest method of getting a controlled frequency response is to use a microphone and a loud-speaker that both have a response approximately independent of frequency over the range concerned, and to incorporate suitable filters in the amplifier The range to be covered is from about 30 c/s up to at least 1000 c/s, and probably up to 4000 c/s

A piezo-electric crystal microphone covers the frequency range satisfactorily, but because of its high impedance it is necessary to keep the capacity of the lead to the first stage of the amplifier low (in the region of 0 0001 microfarad) in order to maintain the response at the upper end of the frequency range The amplifier input impedance must be high, suitable input circuits are given in *Radio Designer's Handbook*, chapter XI It is desirable to separate the amplifier from the microphone so that the latter can be mounted in a small light unit, to be placed directly on the chest High sensitivity to vibrations from the chest-wall, and low sensitivity to air-borne sound and to friction on the case, are required

The loud-speaker must have a response maintained to the lowest audible frequencies, and portability is an advantage It must be free from resonances in the lower audio-frequency range, and must also have a power-handling capacity much greater than the mean power to be broadcast, because the very large amplitude low-frequency components in the heart-sounds, which are almost inaudible themselves because of their low frequency, cause chattering or booming in a small loud-speaker

The amplifier must have a response maintained up to about 4000 c/s, and down to the lowest audible frequencies, though some falling off below 200 c/s is probably required to simulate a stethoscope frequency response Adjustable filters are required to reduce the low-frequency response and simulate a diaphragm stethoscope, and to reduce the high-frequency response and discriminate against extraneous sounds, which tend to have higher frequencies than the wanted sounds Further adjustment of the frequency response is desirable so that an attempt may be made to emphasize a particular sound or murmur The filter and volume controls must be early enough in the amplifier circuit to avoid " limiting " at any stage, but as late as possible, consistent with this, to give quietness in operation These controls should be within reach of the physician who holds the chest piece The distortion-free output of the amplifier need not be as great as the power-handling capacity of the loud-speaker, because the largest amplitudes are at frequencies that are very little heard as sound and do not need to be faithfully reproduced, indeed, a certain degree of relative reduction of the largest amplitudes is probably desirable

Finally, simplicity of operation is important in an equipment to be used for teaching

DESCRIPTION OF THE APPARATUS

Apparatus has been assembled that fulfils very nearly the requirements set out in the previous section The block diagram (Fig 1) indicates the arrangement of the different units A small microphone is used like a stethoscope chest-piece, and its output is carried by 6 feet of rubber-protected screened wire to the pre-amplifier This is housed in a metal box 6 × 6 × 2¼ inches, which also contains the volume control and the tone-control filters This box lies on the bed or a locker, and the three controls, treble, bass, and volume, are operated by rotating knobs Thus all the control can be done by the physician who handles the microphone The output from the pre-amplifier and the power supplies to it are carried by a multi-core cable 11 feet long, connecting it with a larger box 17 × 10 × 9 inches, which contains the main amplifier and all the power supply (The whole apparatus is supplied from A C mains) The output is led to the loud-speaker by 20 feet of twin flex, with an optional extension of another 35 feet The loud-speaker cabinet is of wood, and measures 31 × 18 × 18 inches

Microphone The microphone at present in use consists of a small piezo-electric crystal unit mounted at the apex of a hollow cone turned out of a cylin-
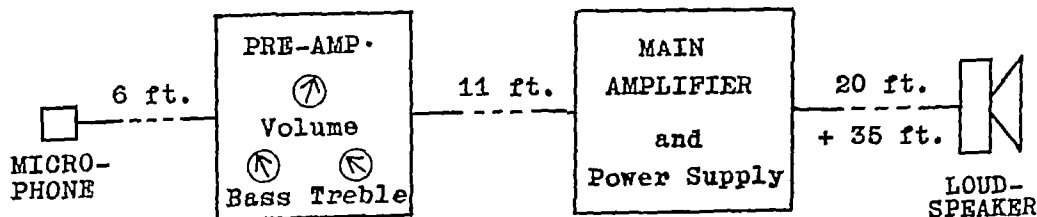
FIG 1 —Block diagram of the complete loud speaker stethoscope

drical block of brass   This is chromium-plated, and is held in the hand in direct contact with the chest   The diameter of the orifice is 1 inch, the total weight is 5 oz   Noises due to friction are no worse than with an ordinary stethoscope   Provided the microphone is in contact with the skin all round its rim, there is little tendency to " howl," and in most cases " howling " is not the factor that limits the maximum useful amplification   The frequency response of this type of microphone (without moving parts other than the crystal itself) can be made practically uniform, but here it is being used with a lower amplifier input impedance than is recommended, which probably reduces the response at the lower frequencies

It is intended to try other types of crystal microphone, as further improvement may still be possible

Amplifier   A high-quality audio-frequency amplifier* was modified to suit the special requirements   It consists of two triode stages as pre-amplifier giving a voltage gain × 850, followed by a filter circuit with treble and bass controls and middle-frequency attenuation − 10 (20db), a potentiometer volume control, an amplifier and phase-splitter stage, and a push-pull power output stage   The amplifier gives an output of 12 watts for an input to the first stage of 20 millivolts r m s   The input impedance (first grid leak) is 1 5 megohm

* The amplifier " QA12/P," supplied by The Acoustical Manufacturing Co Ltd , Huntingdon

The principal modification required was in the filter circuit, which is shown in its final form in Fig 2   It is a resistance-capacity network with separate high-frequency and low-frequency controls, which, in the modified circuit, are not entirely independent in their effects   The frequency response curves for the middle and extreme settings of the two controls are shown in Fig 3 and 4

The filter controls and the volume control are silent in operation   No trouble was encountered from valve noise or microphony   In the cable connecting the pre-amplifier to the main amplifier there was considerable pick-up of hum from H T and L T supplies, which was overcome by additional smoothing in the case of the former, but for the L T a separate transformer was necessary, as spikes at 200 c/s recurrence were generated in the main transformer and were picked up by the signal lead from the heater leads   With these alterations, the hum from the equipment itself is barely audible, and the measured level in an electrical laboratory was 80 mv r m s across the 15-ohm output, part of this being due to pick-up from other sources

Loud-speaker   The loud-speaker is a 15-ohm, 15-watt, 12 inch unit in a special cabinet mounting *   This type of mounting is probably the best to combine robustness and portability with a good low-

* " Labyrinth Loud-speaker, Type SL 15," supplied by The Acoustical Manufacturing Co Ltd., Huntingdon
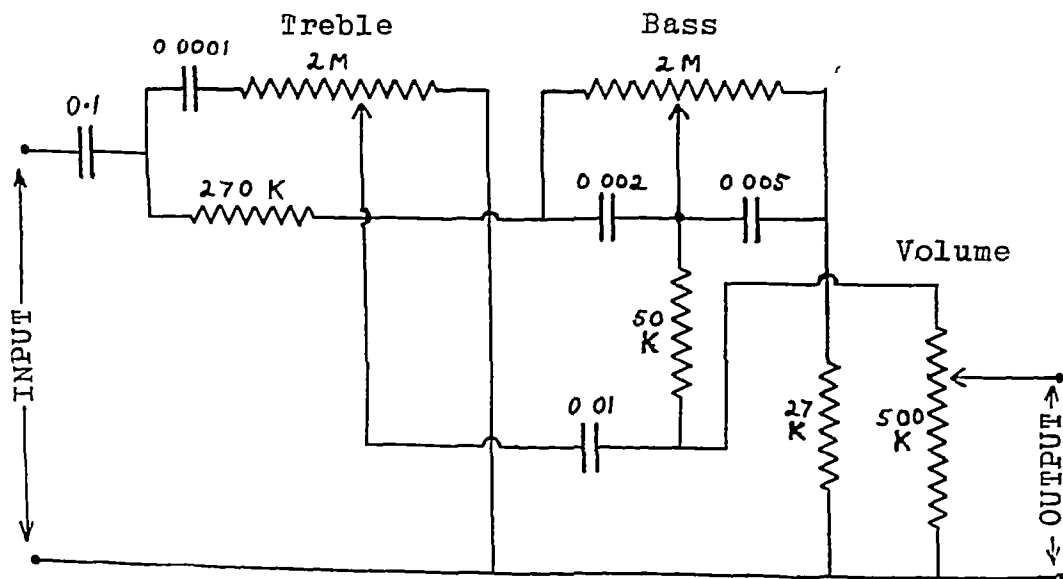
Fig 2 —Full diagram of the filter circuit showing treble, bass, and volume controls   Resistances in thousands of ohms (K) and megohms (M)   Capacities in fractions of a microfarad.
Input   direct from anode of second triode amplifier stage, anode load 100 K
Output   direct to grid of subsequent stage
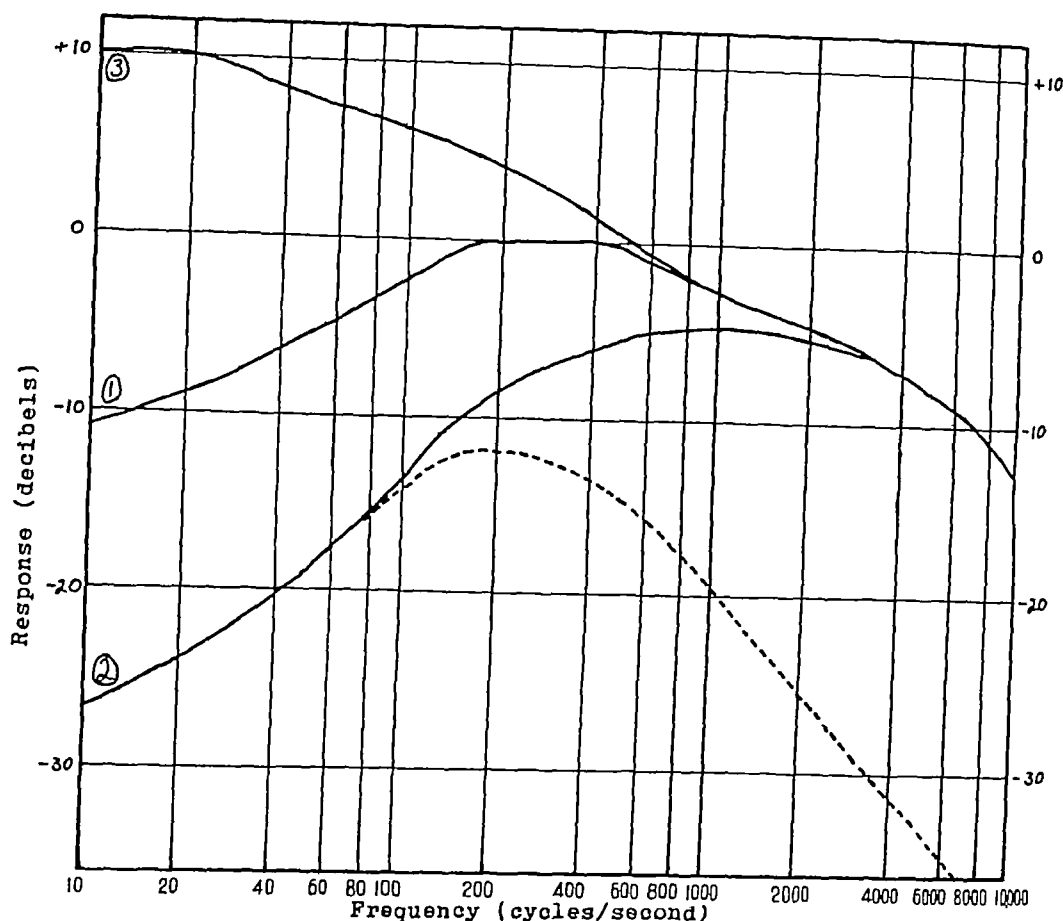
FIG 3 —Frequency response curves of amplifier to show the effect of the bass control

Full curves   treble control central

    (1) *Bass control also central*
    (2) *Bass control set at minimum*
    (3) *Bass control set at maximum*

Broken curve   both controls set at minimum

frequency response   The published performance curve indicates a response that is practically independent of frequency down to 35 c/s, with no significant resonances

There is a slight tendency to boom at the first heart-sound, and this is in most cases the factor that limits the maximum volume consistent with good reproduction

Connection to the loud-speaker is made by means of 20 feet of twin flex, with a jack which is plugged into the main amplifier box   An extension of 35 feet of twin flex is available, with a jack socket at one end and a plug at the other   Each socket is arranged to leave a 15-ohm load across the output

when the corresponding plug is removed, so that there is no danger of leaving the output transformer unloaded

RESULTS

The equipment gives a very close approach to the effect of auscultation with a stethoscope, in a quiet room large enough for twenty people   For auscultation over the præcordium the apparent loudness cannot usefully be increased much above that heard with a stethoscope because distortion of the sounds begins to occur   A variety of pathological murmurs have been listened to, and these as well as the normal sounds are satisfactorily heard   On the whole, very
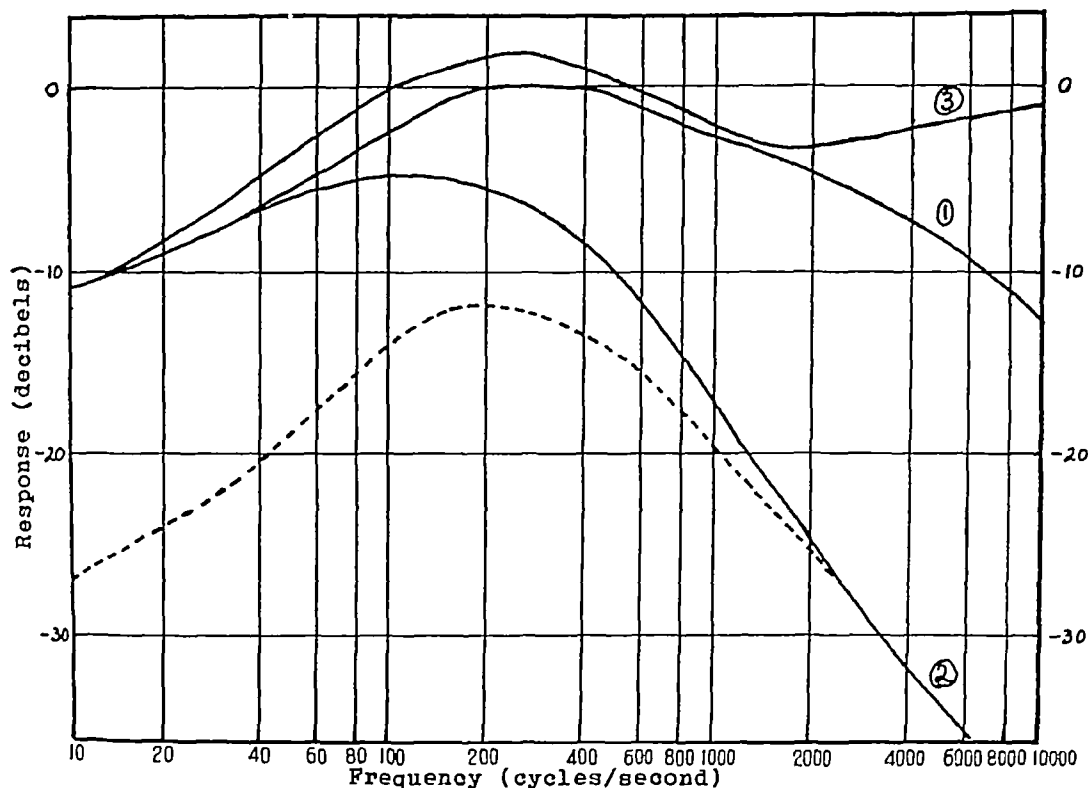
FIG 4 —Frequency-response curves of amplifier to show the effect of the treble control

Full curves   bass control central

    (1) Treble control also central
    (2) Treble control set at minimum
    (3) Treble control set at maximum

Broken curve   both controls set at minimum

faint murmurs are not more easily picked up with the loud-speaker than with a stethoscope, but simultaneous auscultation will allow each student to listen for a much longer time than he would otherwise be able to do, and so increase his chances of picking up a difficult murmur

For auscultation of breath sounds the volume can be considerably increased without distortion, and both normal and pathological sounds are picked up much more easily than with a stethoscope   The volume can then of course be reduced to simulate a stethoscope more exactly

SUMMARY

The problems of electrical amplification of heart sounds and of group auscultation are discussed both theoretically and with reference to previous work

A portable equipment is described which is believed to be suitable for teaching groups of at least twenty students   This consists of a crystal microphone, an electrical amplifier, and a loud-speaker, which have been arranged to give an effect that simulates very closely auscultation with a stethoscope

The amplification, and the high- and low-frequency response of the amplifier, can be easily and silently controlled during auscultation   The relevant frequency response curves are given

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THE EFFECT OF ADENOSINE TRIPHOSPHATE ON THE ELECTROCARDIOGRAM OF MAN AND ANIMALS

BY

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The increasing importance of adenosine triphosphate (*ATP*) in the field of biochemistry demands a close study of its pharmacological properties Earlier work on the lower nucleotides and nucleosides derived from *ATP* showed that these compounds have important effects on the cardiovascular system Now that large amounts of the higher derivatives, such as *ATP*, have become available, it has been shown that the action of these substances is not confined to the cardiovascular system but affects all the organs of the body (Green and Stoner, 1949) Although the effect of these compounds on the heart has been studied in some detail by Drury and his school (1936), their electrocardiographic observations were almost entirely confined to the lower members of the series In the present paper we propose to describe the effects of *ATP* on the electrocardiogram of man and animals The cardiographic method is the only satisfactory one available for the study of changes in cardiac rhythm in man We have also applied this method to the study of the cardiac effects of *ATP* in animals in order to determine the effects of doses higher than those that would have been justifiable in man and also to analyse these actions by procedures impracticable clinically The observations in animals will be reported first, then those in the human subjects, and finally the conclusions arrived at from the combined study

I ANIMAL EXPERIMENTS

Early work on the effect of adenosine and its derivatives on the electrocardiogram has been well reviewed by Drury (1936) It has been shown that these substances affect the conducting system, causing sinus slowing and A-V block In most animals the main effect is upon the S-A node but in the guinea pig the A-V node seems more sensitive

to their action It will be seen that the action of *ATP* is on the whole similar to that of the lower compounds The further actions of *ATP* on the cardiovascular system have been described by us elsewhere (Green and Stoner, 1949)

Methods Experiments were performed on 10 cats and 11 guinea pigs under pentobarbitone sodium (nembutal) anæsthesia The electrocardiogram was recorded with a Sanborn Viso-cardiette In the cat the pressure in the carotid artery was determined with a mercury manometer and respiration recorded by a tambour attached to a tracheal cannula Artificial respiration was used in the majority of the guinea pig experiments All injections were given into the external jugular vein and washed in with 1 5 ml 0 9 per cent sodium chloride from a burette The time of the injection was 1 sec Both the sodium and magnesium salts of *ATP* were used in the animal experiments, the solutions being prepared from *BaATP* (Boots) as described elsewhere (Green and Stoner, 1949) In the observations on man the magnesium salt was used The purity of the *ATP* was checked by chemical analysis and found to be not less than 98 per cent The adenosine used was obtained from British Drug Houses Ltd

RESULTS

Guinea Pig The effect of *ATP* on the conducting system of the guinea pig heart was followed in leads I and II Two dosage levels were used— 0 5 mg and 1 0 mg *MgATP* per kg body weight With the smaller dose the effect on the heart commenced almost immediately after the injection and lasted about 21 seconds, reaching a maximum in 6 to 9 seconds The first effects were on the sinus rate and the P-R interval The sinus rate was reduced by about 18 per cent and the P-R interval

FIG 1 —To be read from left to right and from above downwards   The effect of 0 5 mg *MgATP* per kg body wt , given intravenously, on the electrocardiogram (lead II) of the guinea pig under pentobarbitone (nembutal) anæsthesia   The beginning and end of the injection indicated with arrows   Shows sinus slowing followed by ventricular arrest and 2 1 A-V block

1 mV=1 6 cm   1 sec =2 5 cm

was increased from an average control value of 0 06 to between 0 09 and 0 12 second   At the height of the effect *ATP* exerted a much greater action on the A-V node than on the S-A node and the ventricular beat was completely suppressed for periods of up to 3 seconds   Ventricular beating then returned with 2 1 heart block progressing to normal rhythm (Fig 1)

Despite these marked changes in rhythm the form of the complexes showed little change   The only constant alterations seen were some depression of the P-Q interval giving a spiky appearance to the P waves and increased amplitude of the T waves

After the larger dose of *ATP* the effect attained a maximum at about the same time after the injection and persisted for about 30 seconds   The sequence of events was as before but both the sinus slowing and prolongation of the P-R interval were more marked   The sinus rate was reduced by a maximum of about 36 per cent and the P-R interval was prolonged until at the height of the effect the ventricular beat was suppressed for 6 to 9 seconds   On occasions this was accompanied by atrial asystole   Recovery occurred as before with varying grades of heart block

Changes in the configuration of the complexes were commoner after the larger dose of *ATP*   Increased amplitude of the T wave was evident and low voltage QRS complexes and extrasystoles were also seen   These extrasystoles arose from a focus close to, but below, the A-V node   Occasional abnormalities which were seen, usually during the recovery period, were inversion of the P wave, auricular fibrillation, nodal rhythm, and displacement of the S-T segment

When adenosine was given in equimolecular amounts it had the same effect on cardiac rhythm as *ATP*   Section of the vagi in the neck did not alter the response to *ATP* or adenosine

Cat   The effect of *ATP* on the electrocardiogram (lead II) of the cat was studied after the intravenous injection of 1 0 mg and 2 0 mg *MgATP* (0 3–0 5 and 0 7–1 0 mg per kg body weight)   The effects observed differed somewhat from those in the guinea-pig and more closely resembled those to be described in man

The main effects after the smaller dose of *ATP* were sinus bradycardia and lengthening of the P-R interval   The degree of sinus slowing varied but at the height of the effect, about 10 seconds after

injection, the sinus rate was usually decreased by about 50 per cent The effect persisted for a further 10 to 20 seconds by which time the rate had returned to normal The P-R interval increased from 0 06 to 0 09 second at the height of the effect The P-Q interval was depressed and changes constantly occurred in the T wave In the majority of experiments the T wave was increased in amplitude during the first 10 seconds after the injection Sometimes this change persisted for as long as 42 seconds and was accompanied by alterations in the level of the S-T segment (Fig 2) In other experiments, during the later stages of the ATP action, the T waves were depressed and then inverted

FIG 2 —Segments of the electrocardiogram (lead II) record immediately before (A), and 15 sec after (B), the intravenous injection of 2·0 mg MgATP into a cat (3 0 kg body wt) under pentobarbitone (nembutal) anæsthesia, showing the depression of the S-T segment

1 mV=1 6 cm   1 sec =2 5 cm

Similar but more marked changes occurred after the larger dose (Fig 3) Here the P-R interval was increased from an average control value of 0 07 to 0 11 second Sinus bradycardia, which was still the main effect, was more pronounced sometimes leading to complete asystole, in one experiment there was complete asystole for 6 seconds with ventricular asystole for 11 seconds The maximum effect occurred about 10 seconds after the injection and was characteristically heralded by a run of about four extrasystoles (Fig 4) arising from a focus close to, but below, the A-V node The T wave changes were of the same type as before but were more evident after these larger doses

Previous work has shown that the vagus is concerned in the cardiovascular response to ATP in the cat (Bielchowsky, Green, and Stoner, 1946) In this animal section of the vagi in the neck or atropinization diminished the effect of ATP on both the blood pressure and the heart, but the blood pressure changes were much less affected than one would have expected from the changes in the cardiac response (Fig 5) For instance, in one experiment

where the depressor response to 2 0 mg MgATP was 35 mm Hg before vagal section, the P-R interval was prolonged from 0 06 to 0 10 second, and the sinus rate slowed from 180 to 60 beats a minute with complete A-V dissociation for 3 seconds After vagal section the same dose only prolonged the P-R interval very slightly, from 0 06 to 0 08 second, and slowed the sinus rate only from 160 to 140 beats a minute without dissociation, nevertheless the blood pressure fell by as much as 22 mm Hg Although inactivation of the vagi greatly reduced the effect of ATP on cardiac rhythm it did not alter its action on the configuration of the complexes nor prevent the appearance of extrasystoles

Prostigmine had the opposite effect to vagal section and greatly potentiated the action of ATP on cardiac rhythm in the cat (Fig 6) In a normal cat 2 0 mg MgATP, injected intravenously, lengthened the P-R interval from 0 08 to 0 12 second, and produced complete asystole for 3 seconds In the same cat, after intravenous injection of 0 125 mg prostigmine, the same dose of MgATP lengthened the P-R interval from 0 11 to 0 14 second and produced complete asystole for 18 seconds followed by a slow return to normal beating At the same time the depressor response was increased This effect of prostigmine could be prevented by vagal section

In the cat the rate changes produced by ATP were not reproduced by equimolecular amounts of adenosine until after section of the vagi when the effects were similar

Effect of Magnesium The influence of intravenous magnesium sulphate on the response to ATP was tested in both guinea pig and the cat in view of previous work on the effect of this ion on nucleotide action (Green and Stoner, 1944, Bielchowsky, Green, and Stoner, 1946) The alteration in the response after Mg was more easily interpreted in the guinea pig since the vagus is not implicated in that animal As shown in Table I, the effect of intravenous magnesium sulphate was to increase the effect of ATP on the cardiac rhythm Mg^{++} had a similar influence on the action of ATP on the cardiac rhythm of the cat but in that animal the effect was complicated by the anæsthetic action of Mg^{++} on the vagus Small doses of Mg^{++}, however, increased the effect of ATP on the P-R interval and the duration of the effect The prolongation of the action of ATP on cardiac rhythm was not the only effect of Mg^{++} on the ATP response, since it also prevented the appearance of extrasystoles

Effect of Antimalarial Drugs Raventos (1948) has recently postulated that there is an antagonism between adenosine and the antimalarial group of
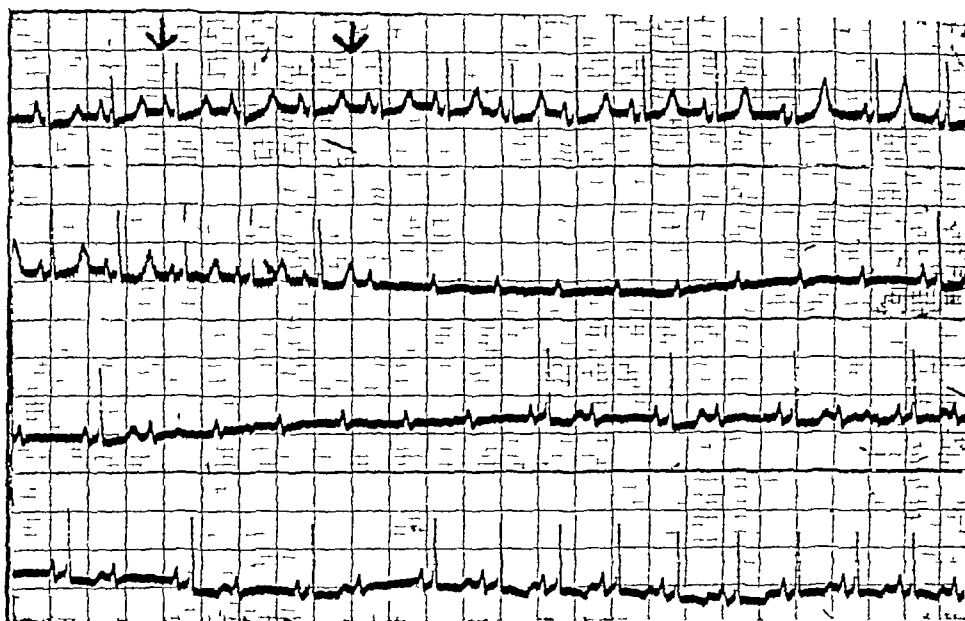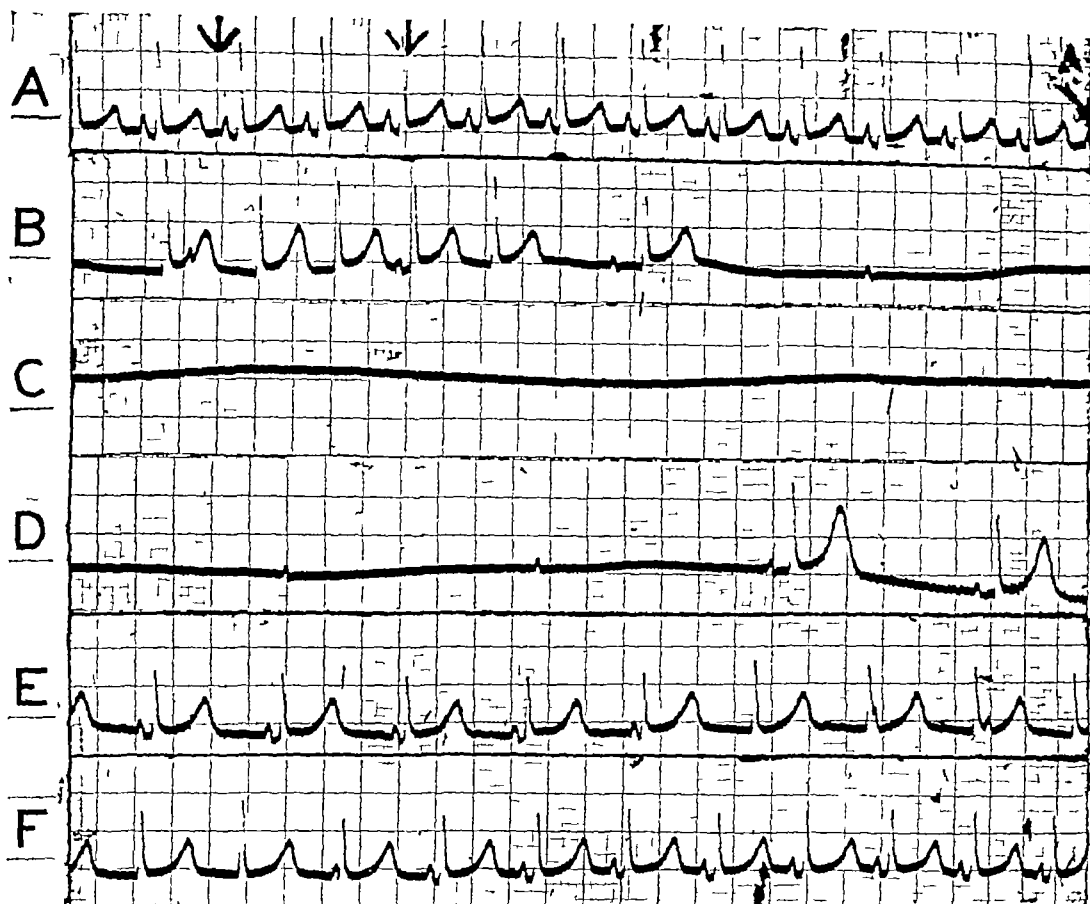
FIG 3 —To be read from left to right and from above downwards   The effect of 2 0 mg *MgATP* given intraven ously on the electrocardiogram (lead II) of the cat (2 9 kg body wt) under pentobarbitone anæsthesia   The beginning and end of the injection is indicated with arrows   Shows sinus slowing, ventricular asystole and complete asystole with nodal rhythm during the recovery period

(A)	0–5 sec	(D)	22–27 sec
(B)	11–16 sec	(E)	45–50 sec
(C)	16–22 sec	(F)	55–60 sec

1 mV=1 6 cm   1 sec =2 5 cm

drugs since he found that the cardiac effects of adenosine were less after the previous administration of quinine, mepacrine, pamaquin, and paludrine In the guinea pig heart lung preparation he found that paludrine, added directly to the circulating blood, did not antagonize the action of adenosine but that the blood of guinea pigs treated with paludrine did have this effect

In part we have been able to confirm these findings In the cat, the intravenous or intramuscular injection of quinine sulphate (25 mg per kg body weight) does decrease the effect of *ATP* on the heart and blood pressure   In the guinea pig also, quinine sulphate (15 mg per kg body weight) decreases the effects of adenosine and *ATP* on the heart   In our hands paludrine hydrochloride has behaved differ ently and when doses in the therapeutic range have been given intravenously over a period of half an hour no change was observed in the electrocardiographic response to *ATP* in the cat or guinea pig   It was only when the dose was raised to the limits of tolerance (60 mg per kg body weight) that any alteration in the response was observed and then the changes were only slight and equivocal
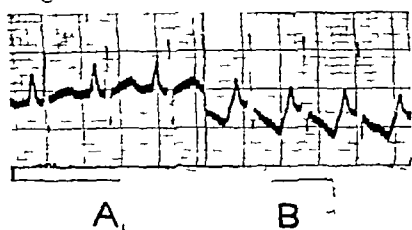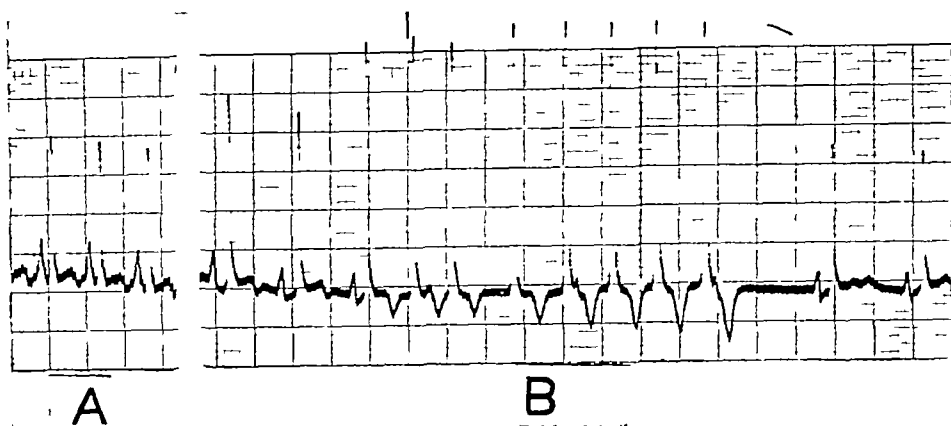
FIG 4 —Segments of the electrocardiogram (lead II) record immediately before (A), and 5 sec after (B), the intravenous injection of 2 0 mg *MgATP* into a cat (2 1 kg body wt) under pentobarbitone (nembutal) anæsthesia   Shows the characteristic run of nodal extrasystoles preceding the full action of the *MgATP*

1 mV=1 c cm   1 sec =2 5 cm
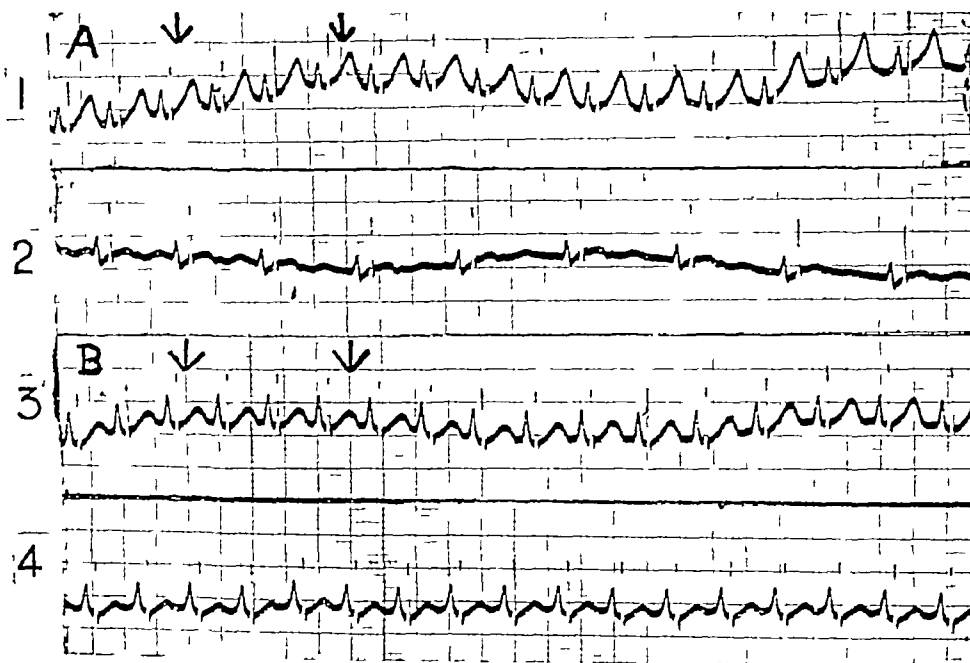
FIG 5 —To be read from left to right and from above downwards   The effect of 2-0 mg *MgATP* given intravenously on the electrocardiogram (lead II) of a cat (2 7 kg body wt) under pento-barbitone (nembutal) anæsthesia, (A) before and (B) after the intravenous injection of 0 75 mg atropine sulphate per kg body wt   The beginning and end of the injection of *MgATP* indicated with arrows

(1) 0–5 sec   (2) 11–16 sec   (3) 0–5 sec   (4) 11–16 sec

Shows the decrease in the degree of sinus slowing produced by *MgATP* after paralysis of the vagus

1 mV=1 6 cm   1 sec =2 5 cm

TABLE I

THE EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE ON THE CARDIAC RESPONSE TO *ATP* IN THE GUINEA PIG

Dose No	Duration of effect (sec)	P-R interval (sec)		Sinus rate Beats per minute		Ventricular rate Beats per minute	
		Before Injection	After Injection	Before Injection	After Injection	Before Injection	After Injection
1	18	0 06	0 09	220	180	220	80
2	18	0·06	0 09	200	180	200	100
3	31	0 11	0 16	120	60	120	20
4	36	0 10	0 18	120	80	120	0

The table shows the effect of successive doses of *MgATP* (0 5 mg per kg body weight) on the P-R interval, and sinus and ventricular rates, before and after intravenous doses of magnesium sulphate

Between doses No 2 and 3, 3 0 ml MgSO$_4$ 0 154 M given i v and between doses No 3 and 4, 2 0 ml MgSO$_4$ 0 154 M i v
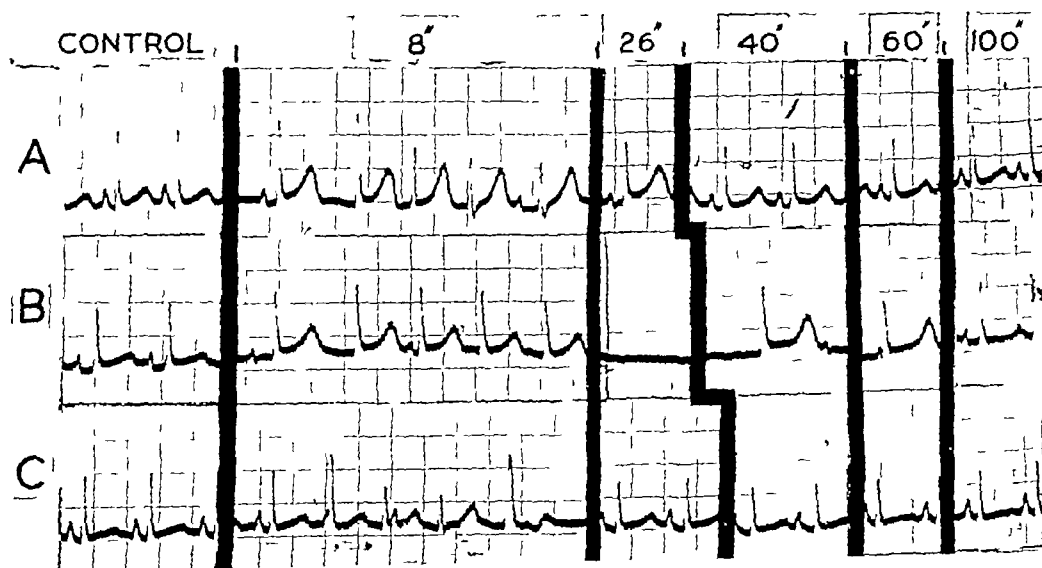
FIG 6 —Segment of the *electrocardiogram* (lead II) record immediately before (control) and at stated intervals after the intravenous injection of 2 0 mg *MgATP* into the same cat (2 7 kg body wt) in nembutal anæsthesia under varying conditions

(A) Effect of *MgATP* alone
(B) After intravenous injection of 0 125 mg prostigmine
(C) As for (B) except that both vagi have been divided

Shows the great increase in the effect of *ATP* after prostigmine administration, which is prevented by division of the vagi

1 mV = 1 6 cm   1 sec = 2 5 cm

II OBSERVATIONS ON *HUMAN SUBJECTS*

The effect of adenyl compounds on the human heart has been comparatively little studied Honey, Ritchie, and Thomson (1930) showed that adenosine could produce heart block in healthy men and von den Velden (1932) that adenylic acid would give bradycardia Richards (1934a) studied the effects of both adenylic acids and adenosine on the blood pressure and electrocardiogram He concluded that the blood pressure is unaffected but that in some individuals heart block can be produced by

either compound Stoner and Green (1945) using the sodium and magnesium salts of *ATP* produced a rise of pulse rate with small doses and a rise followed by a large fall with large doses Electrocardiograms were not taken but heart block was suspected in one case The systolic blood pressure was raised during the period of tachycardia and fell slightly during the time when the pulse was slowing Arteriolar dilatation occurred with a consequent rise of skin temperature

ATP in the Treatment of Rheumatoid Arthritis Lövgren (1945) has claimed that *ATP* has a beneficial effect on cases of rheumatoid arthritis " Adynol," a crude preparation containing 50 to 60 per cent *ATP*, was given by intravenous injection in doses of 30 to 45 mg or by intramuscular injection in doses of 7 5 to 30 mg We decided to treat a series of cases with a purer preparation of *ATP* and at the same time to study the effect of this substance on the cardiovascular system

The results of treatment of rheumatoid arthritis were most disappointing Courses of daily injections of *MgATP* in doses of 15 to 30 mg were given for periods up to three months to 15 patients Several cases improved subjectively but we could not convince ourselves that there was any change in the degree of disability that would not have been obtained by simple rest in bed and physiotherapy There was no significant alteration in the erythrocyte sedimentation rate

Since, as will be shown, *MgATP* has a profound effect on the conducting system of the heart and since it was desired to give to each patient the maximum tolerated dose, very frequent electrocardiographic observations were made on each case These will now be reported

Plan of Investigation Seven patients (6 male and 1 female), all with normal hearts, were chosen from the 15 treated for arthritis and were observed specifically for electrocardiographic changes immediately after injection The patient rested comfortably on a couch, and control blood pressure readings and cardiograms were taken *MgATP* was injected intravenously, taking 6 to 12 seconds over the injection Blood pressure readings were taken at 15-second intervals, until the figures returned to pre injection levels Cardiograms were taken at the same time as the injection and continued for 1 minute and then for 10 seconds at half-minute intervals for a further minute Small doses of 5 mg were used initially on each patient and gradually increased by 5 mg at each injection up to the maximum tolerated dose which varied from 15 to 40 mg (0 21–0 57 mg per kg body weight) In all, 100 tracings were obtained in this manner from the 7 patients selected

EFFECTS OF INJECTION

(1) *Subjective* These were remarkably constant with doses above 10 mg Ten to fifteen seconds after starting the injection, the subject noted a sharp taste in the mouth, which was followed by hyperpnœa, cough, and obvious flushing of the face with a brief sensation of faintness and throbbing in the head All these effects had disappeared by the end of the first minute and were much less marked if the injection was made slowly

(2) *Blood pressure* Thirty observations were made on four cases with doses above 10 mg A fall of blood pressure invariably occurred, the maximum being 100 mm Hg with doses of 35–40 mg and was usually greatest about 15 to 20 seconds after the beginning of the injection The blood pressure recovered rapidly so that two minutes later it was at or above the pre-injection level It is hardly surprising that very low readings were obtained in cases in which asystole or pronounced bradycardia occurred but in several instances with doses giving only sinus slowing, significant falls of pressure were recorded which we attributed to arteriolar dilatation In general, the fall in systolic pressure was greater than in diastolic pressure but the latter is difficult to determine accurately in observations of this type The fall in systolic pressure was considerably greater than that previously recorded (Stoner and Green, 1945)

(3) *Changes in the Electrocardiogram* Lead II was used throughout the observations

The effects of a given dose differed greatly in different patients but in the same patient, the response was sufficiently constant to enable variations produced by other procedures to be assessed We did not observe the development of tolerance In our observations on the effects of drugs, we always made at least one control observation immediately before giving the drug and one after the effect of the drug had worn off We also always used samples of *ATP* from the same batch

Small doses (5–15 mg) of *MgATP* produced a sinus tachycardia preceded by a short period of sinus slowing Larger doses (15–30 mg) gave marked sinus slowing and always affected the conducting tissues producing first or second degree A-V block (Fig 9A and C) Wenckebach periods were often observed (Fig 10A) Maximum doses (30–40 mg) produced similar changes of greater intensity with an increase in the duration of heart block and in the number of dropped beats Ventricular standstill (Fig 7) and complete asystole were observed in two patients These effects are similar to those seen in the guinea pig (Fig 1) The results in Case 1 are summarized in Table II

With the doses used, changes in the shape of the
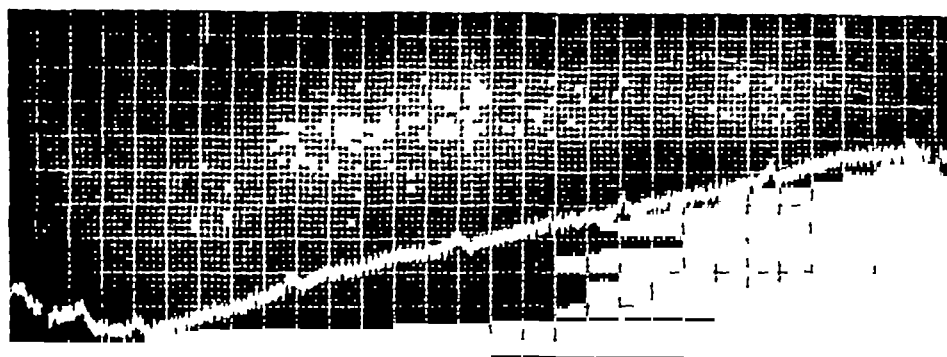
FIG 7—Case IV Effect of intravenous injection of *MgATP* on the electrocardiogram (lead II)
Shows ventricular standstill for 5 5 sec occurring 14 sec after injecting 19 mg *MgATP*

1 mV = 1 cm   1 sec = 2 5 cm

TABLE II

RESULTS OBTAINED IN CASE I

Dose of *MgATP* (Mg)	Other drugs	Maximum increase in P–R interval (Sec)	Wenckebach phenomenon	Number of dropped beats	Duration of block (Sec)	Sinus slowing	Remarks
30	—	0 20	+	1	6	+	Typical single observation
30	—	0 14	—	1–2	8	+	Mean of 7 observations
30	After 400 mg mepacrine orally	0 05	—	0	2 5	+	
30	After 100 mg paludrine orally	0 22	—	1	9	+	
35	—	0 28	+	1	9	+	
35	—	0 16	+	1–2	6	+	Mean of 5 observations
35	After 1 2 mg atropine intravenously	0	—	0	0	+	
35	After 2 4 mg atropine intravenously	0	0	0	0	+	
40	—	0 14	+	1	10	+	
40	—	0 16	+	1–0	7 5	+	Mean of 2 observations
40	After 1 g quinidine sulphate orally	0 06	—	1	2	++	
40	After 3 g quinine hydrochloride orally	0-04	—	0	0	++	

Table II shows the effects of *MgATP* on the heart and the effects of mepacrine, paludrine quinidine, quinine, and atropine on the cardiac response to *MgATP*
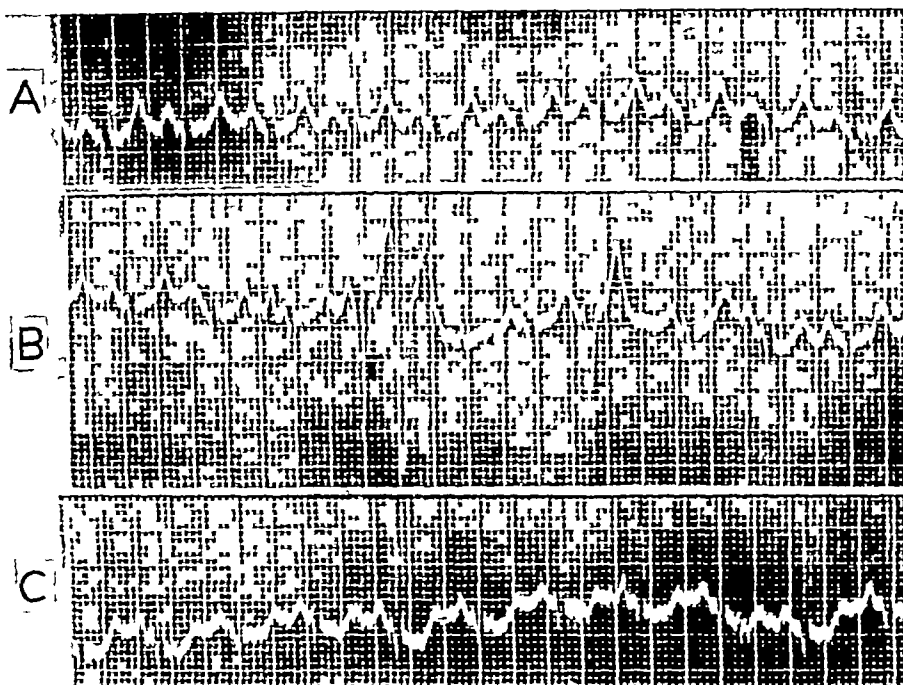
FIG 8 —Case VII   Effect of intravenous injection of *MgATP* on the electrocardiogram (lead II)

    (A) Before injection showing sinus tachycardia
    (B) 16 sec after injection of 15 mg *MgATP* showing 3 ventricular extrasystoles
    (C) 26 sec after the same injection, showing depression of the S–T segment

       1 mV=1 cm   1 sec =2 5 cm

complexes were not produced as consistently as in the observations on animals   In Case 3, with doses of 20 to 30 mg , the P wave was depressed, a small Q wave appeared and the T wave became isoelectric or inverted   In Case 7, with doses of 10 to 15 mg , premature ventricular contractions were observed and later the S–T interval was significantly depressed   Heart block did not occur in this case with these doses and it was thought inadvisable to increase them   The curves from this case which were obtained on three separate occasions resemble closely those obtained in the cat (compare Fig 2 and 8)

Comparison of MgATP and Adenosine   The effects of adenosine and *MgATP*, given in equimolecular amounts, were compared in 2 subjects (Cases 1 and 2)   It was found that although adenosine produced the same type of change in cardiac rhythm as *MgATP* it was not as active

OBSERVATIONS ON THE RESPONSE TO *ATP* AFTER THE INJECTION OF OTHER DRUGS

These observations fall into two main groups

Firstly an attempt was made to see whether the effects of magnesium sulphate and of vagal inactivation by atropine on the response to *ATP* in man were the same as those we had encountered in animals   The effects of adrenaline and quinidine were also investigated, the former because it is known to facilitate conduction down the bundle (Wiggers, 1927) and the latter because it might have been expected to increase the degree of conduction defect as in clinical cases of heart block (Lewis, 1925) Secondly, we investigated the effect of various antimalarial drugs on the response of the human heart to *ATP* in view of the animal experiments of Raventós which we had partially confirmed

Magnesium Sulphate   This substance was given intravenously in a doze of 1 6 g $MgSO_4$ 7 H_2O (8 ml of 20 per cent solution) to 2 subjects, 7 to 10 minutes before the injection of *MgATP*   In both, there was a definite increase in the degree of heart block produced by *MgATP*   The results therefore resemble those obtained in animals

Adrenaline   Injections of *MgATP* were given to 2 subjects 5 minutes after an intramuscular injection
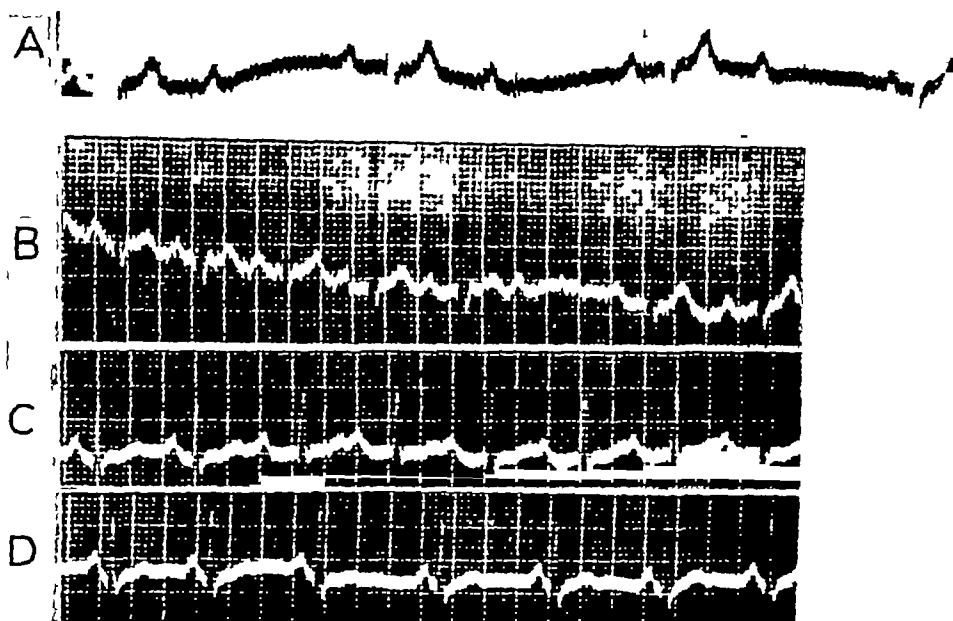
FIG 9 —Effect of *MgATP* on the human electrocardiogram before and after intravenous injection of atropine

    (A) Case IV, 15 sec after injection of 17 mg *MgATP*
    (B) Case IV, 15 sec after injection of 17 mg *MgATP*   Five minutes previously 2 5 mg atropine sulphate had been given intravenously
    (C) Case I, 15 sec after injection of 35 mg *MgATP*
    (D) Case I, 18 sec after injection of 35 mg *MgATP*   Five minutes previously 1 2 mg atropine sulphate had been given intravenously

    Both cases show reduction in the degree of heart block due to *MgATP* after atropine administration   Sinus slowing is still seen

$$1 \, mV \approx 1 \, cm \qquad 1 \, sec \approx 2 \, 5 \, cm$$

of 0 5 ml 1 1000 adrenaline hydrochloride and to 1 subject after 1 0 ml   The number of dropped beats and the duration of the block was reduced in each instance

    Atropine   After control observations, 5 subjects were given atropine sulphate intravenously in doses usually considered sufficient to produce complete vagal paralysis   When the heart rate had risen to a stationary level, *MgATP* was given   Sinus slowing still occurred, but in two instances second degree A-V block was completely prevented   In the other observations the degree and duration of heart block was much less (Fig 9 and Table II)

    Quinidine   Two subjects (Cases I and VI) received 1 g of quinidine sulphate in divided doses, the last dose of 0 2 g being given half an hour before the injection of *MgATP*   The increase in P–R interval and the duration of heart block were significantly less than in the control observations

(Fig 10 and Table II)   The degree of sinus slowing was the same

    Antimalarial drugs   1 *Quinine*   Three grammes of quinine hydrochloride were given orally over 3 days to 4 subjects (Cases 1, 2, 4, and 6), the last dose being administered half to two hours before the injection of *MgATP*   The effects were similar to those obtained using quinidine and in one case A-V block was almost completely prevented (Fig 10E and Table II)

    2 *Mepacrine*   Three subjects (Cases 1, 2, and 6) received 0 4 g mepacrine hydrochloride by mouth over thirty-six hours, the last dose of 0 2 g being given two hours before the injection of *MgATP* The degree and duration of heart block were significantly less than in control observations (Fig 10B and Table II)

    3 *Paludrine*   Three subjects (Cases 1, 2, and 6) were given 100 mg. paludrine hydrochloride by
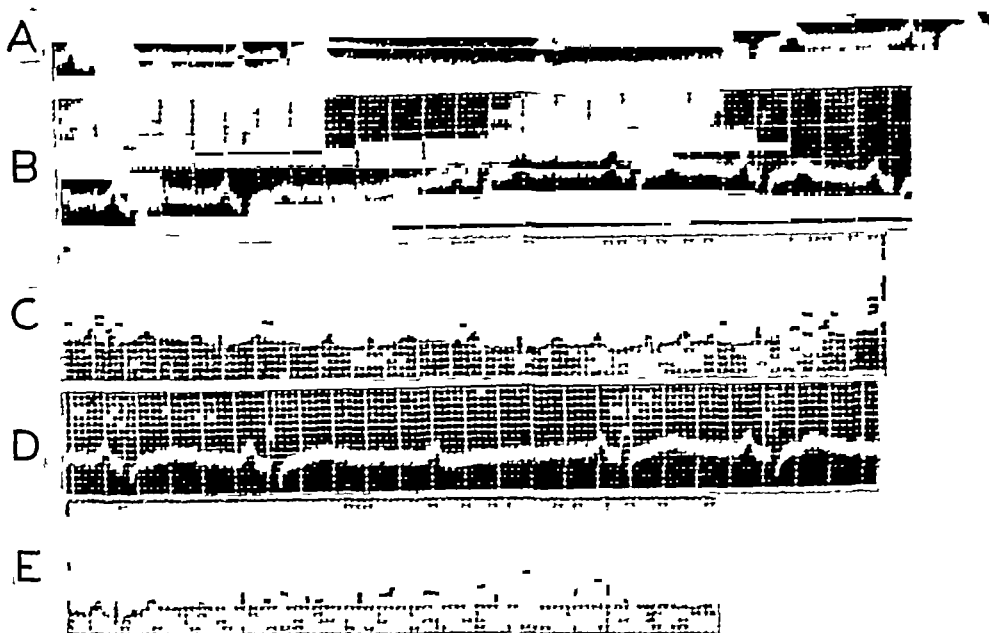
FIG 10 —Case I Effect of mepacrine, quinidine, and quinine on the response to the intravenous injection of *MgATP* (lead II)

(A) Control, 17 sec after injection of 30 mg *MgATP* Normal P-R interval for this case lay between 0 16 sec and 0 18 sec
(B) Effect of mepacrine (for dosage, see text) 18 sec after injection of 30 mg *MgATP*
(C) Control, 17 sec after injection of 40 mg *MgATP*
(D) Effect of quinidine (for dosage, see text) 16 sec after injection of 40 mg *MgATP*
(E) Effect of quinine (for dosage, see text) 17 sec after injection of 40 mg *MgATP*

Shows the reduction in the effect of *ATP* after certain antimalarial drugs

1 mV=1 cm   1 sec =2 5 cm

mouth and one (Case 4) 200 mg three hours before injection of *MgATP* No reduction in the degree of block was noted Indeed, in Case 4 the block persisted much longer than in control observations We thought it inadvisable to investigate the effects of higher doses, because of toxic symptoms produced by the dosage given to Case 4

DISCUSSION

These observations show that *ATP* has a profound effect on the conducting system of the heart causing changes in cardiac rhythm similar to those described for adenosine and muscle adenylic acid by Drury and Szent-Gyorgyi (1929) The action is essentially a depression of normal function with sinus slowing, prolongation of the P-R interval and the appearance of heart block With sufficiently large doses this A-V block may be complete and complete asystole can also occur In man these effects were often followed by a short period of sinus tachycardia but

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the second phase of sinus bradycardia described by Drury and Szent-Gyorgyi (1929) was seldom seen in our observations, perhaps because we used smaller doses With very small doses of *MgATP*, sinus tachycardia was (sometimes) the only effect produced For the most part the effect of *ATP* was similar in the three species studied but there were certain interesting minor differences Drury (1936) has emphasized that the site of the main action of the adenyl compounds differs in different species As with the lower compounds, the main action of *ATP* in the guinea pig is upon the A-V node whereas in man and the cat, especially in the latter, the main effect is upon the S–A node An illustration of this is the more frequent occurrence of complete asystole in the cat than in the guinea pig

McDowall (unpublished report to the Medical Research Council, 1944) first pointed out that the vagi participated in the cardiovascular response to *ATP* in the cat and this has been fully confirmed by

us both here and elsewhere (Bielchowsky, Green, and Stoner, 1946, Green and Stoner, 1949)   We found that amongst the common laboratory animals this reaction was only seen in the cat and that in this animal it was only *ATP* which acted in this way The present studies, in addition to giving some information on the efferent mechanism of this reflex, also show that the vagi are similarly involved in man   Experiments on the vagotomized cat indicate that the sinus bradycardia after *ATP* is in part due to its action through the vagi   In man, with the vagi paralysed by atropine, the reduction in the degree of sinus slowing was not so marked but the elimination of the A-V block was very striking

Direct comparison of the changes in cardiac rhythm produced by equimolecular amounts of adenosine and *ATP* showed that the effects were the same in the guinea pig but not in the cat or man, i e in the two species where the vagus is involved   A similar effect was, however, seen in the cat after the vagi had been divided   These findings are in agreement with those on the isolated perfused rabbit's heart (Green and Stoner, 1949) which showed that the effect of these compounds on the conducting system is essentially due to their adenosine content

Alterations in the cardiac rhythm are not the only changes seen after the injection of *ATP* Various other changes occurred, notably ventricular extrasystoles and displacement of the S–T segment, which are best attributed to a direct action on the myocardium   This effect is not seen after adenosine for as Drury (1932) and Green and Stoner (1949) have shown it is only the phosphorylated derivatives which possess this action

That *ATP* has this action on the myocardium may be of some practical importance   Adenosine and muscle adenylic acid, often mixed with other substances in the form of tissue extracts, have been widely used in the treatment of cardiac and peripheral vascular disease   The alleged beneficial effects have been attributed to vasodilatation of the coronary and peripheral vessels and to a direct action on the myocardium   It seems improbable that, in the doses given and using the routes of administration advised, beneficial results would be likely to ensue   But, in view of the greater general activity and more definite role of *ATP* in muscle metabolism, it is probable that attempts will be made to use this substance in the therapy of cardiovascular disease   In view of the ectopic beats and alterations in the S–T segment observed by us this would seem unjustifiable   If it is given in the treatment of other types of disease it should be given by slow intravenous injection or intramuscularly Unfortunately, when given by the latter route the

dose must be large and absorption is irregular

It is of great interest that the cardiac effects of *ATP* are capable of being influenced by the previous administration of other substances, one of the most important of which is Mg^{++} The striking effect of this ion in increasing the shock-inducing action of *ATP* and altering its action on the cardiovascular system have been dealt with elsewhere (Green and Stoner, 1944, Bielchowsky, Green, and Stoner, 1946)   The electrocardiographic observations de scribed here show that Mg^{++} administration in creases the effect of *ATP* on the conducting system whilst decreasing its effect on the myocardium Similar effects were observed in experiments on the isolated perfused rabbit's heart   This phenomenon is thought to be due to the interference of Mg^{++} in the enzymic breakdown of *ATP* (Green and Stoner, 1949)

Although *ATP* has such a powerful effect on the conducting system of the heart it would seem that this action can still be antagonized by adrenaline This action of adrenaline in facilitating conduction through the bundle has been subject to very little experimental investigation in the past largely due to the difficulties of producing graded heart block under experimental conditions   Our observations, therefore, may indicate an approach to this problem

Quinine, quinidine, and mepacrine also clearly hinder the development of the *ATP* effect but it is not at all clear why they should have this action Indeed one might have expected *ATP* to have had a greater effect after the administration of these compounds   Our failure to elicit a similar effect with paludrine even when, in animals, very large doses were given, prevents us from agreeing with Raventós (1948), that there is an antagonism between the antimalarial drugs and the cardiac effects of the adenyl derivatives   The antagonism would seem to be between these compounds and certain members of the quinoline and acridine series   The further aspects of this antagonism are dealt with elsewhere (Green and Stoner, 1949)   Whilst no explanation of the mechanism involved can yet be given there is no evidence to suggest that it is due to the interference of these quinoline and acridine deriva tives in the metabolism of nucleotide

SUMMARY

The effect of the intravenous injection of adenosine triphosphate (*ATP*) on the electrocardiogram has been studied in human subjects, cats and guinea pigs

The effect of *ATP* on cardiac rhythm varies with the dose   Whilst very small doses may give sinus tachycardia, the normal effect is to cause sinus slowing, prolongation of the A-V interval and second degree A-V block   Large doses frequently

cause standstill either of the ventricles or the whole heart

ATP acts mainly on the S–A node in the cat and man but mainly on the A-V node in the guinea pig

It has been shown that part of the *ATP* effect in the cat and man is mediated through the vagus

Equimolecular amounts of adenosine will reproduce the effect of *ATP* on cardiac rhythm in the guinea pig and also in the cat if the vagi are first inactivated

The effects of *ATP* are not confined to cardiac rhythm, and other changes in the electrocardiographic complexes were seen in both man and animals which were thought to be due to a direct action on the myocardium   These changes were not seen after adenosine

The effect of the previous administration of certain compounds on the response to *ATP* was also observed with the following results

(1) *Magnesium sulphate* increased the effect on cardiac rhythm and decreased the action on the myocardium

(2) *Adrenaline* shortened the period of heart block

(3) *Quinine, quinidine, and mepacrine* all decreased the effect on cardiac rhythm

(4) *Paludrine* had no significant effect on the response

ATP administered intravenously for periods up to three months produced no significant improvement in 15 cases of rheumatoid arthritis

The significance of these observations and their relationship to other of our findings has been discussed

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FAMILIAL CARDIOMEGALY

BY

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When valvular, hypertensive, and congenital heart disease have been excluded as causes of cardiac enlargement, some rarer condition should be sought, but only after excluding bradycardia, pericardial disease, sternal depression, or an elevated diaphragm, which by themselves without real enlargement produce an exaggerated cardiac silhouette on cardioscopy Such being eliminated, there remains a group where the cause of cardiac enlargement is obscure, and it is the purpose of this paper to describe cases with common subjective and objective symptoms, and to propose a syndrome that serves to explain a hitherto ambiguous form of cardiac enlargement and facilitates clinical diagnosis of the condition

NOTES OF THREE CASES IN ONE FAMILY

Case 1 Male, aged 18 years He was referred by a service medical board which sought an explanation for the displacement of his apex beat He admitted to no symptoms at the time and he appeared to be a well-developed healthy youth The pulse was irregular from extrasystoles with brief periods of paroxysmal tachycardia The blood pressure was 120/80 The apex beat was forcible and was displaced as far as the left anterior axillary line The heart sounds were clear and there were no murmurs A triple rhythm was present from the addition of the third heart sound There was no enlargement of the liver or spleen, and further examination found no abnormal signs elsewhere including the central nervous system The Wassermann reaction was negative The blood sugar and cholesterol were both normal, and so was the sugar tolerance test, there was no ketosis The cardiogram (Fig 1) showed extrasystoles and exceptionally wide QRS complexes with inverted T waves On cardioscopy (Fig 3) there was great enlargement of the heart, and particularly of the left ventricle, the border of which was remarkably quiet compared with the mobile right auricle

While under observation for two months, the extrasystoles became more frequent and when attacks of paroxysmal tachycardia increased in number and severity, the patient was handicapped in his work at times by giddiness At last, when tachycardia (Fig 2) persisted for two days, pulmonary œdema (Fig 4) developed and he died on the third day

Summary of Necropsy (*P M* 121/1947) By Professor Dorothy Russell of the Bernhard Baron Institute of Pathology

Acute pulmonary œdema Heart failure Familial Cardiomegaly Clear yellow pericardial effusion (4 oz.) Slight whitish opacity of most of visceral pericardium over both ventricles Milk-spot (2 5 by 1 2 cm) on anterior surface of right ventricle Foramen ovale patent (about 1 cm diameter), the orifice being valvular Great thickening (up to 4 cm) of myocardium of left ventricle, without appreciable dilatation, composed of pale brown moderately firm tissue blotched with numerous ill defined pale areas of fibrosis (Fig 5) Similar proportionate thickening of other chambers of heart (Fig 6), but least marked of left auricle (5 cm diameter, 0 4 cm thick) All valves normal apart from congenital fenestration of two pulmonary cusps Coronary arteries normal and enlarged in proportion to ventricles, no atheroma Aorta of normal circumference (6 cm at ring, and 0 2 to 0 25 cm thick) Very slight atheroma Early mucinous degeneration of media of aorta found microscopically

Clear yellow pleural effusions (right, 12 oz., left, 5 oz.) Almost solid œdema of right lung, showing microscopically variable numbers of red corpuscles and phagocytes in alveolar spaces, purulent bronchitis and early broncho-pneumonia present in a few places Left lung similar but showing, microscopically, a layer of fibrin coating respiratory bronchioles and some alveoli Enlargement of gland at tracheal bifurcation, and another above right bronchus, by miliary and larger caseous

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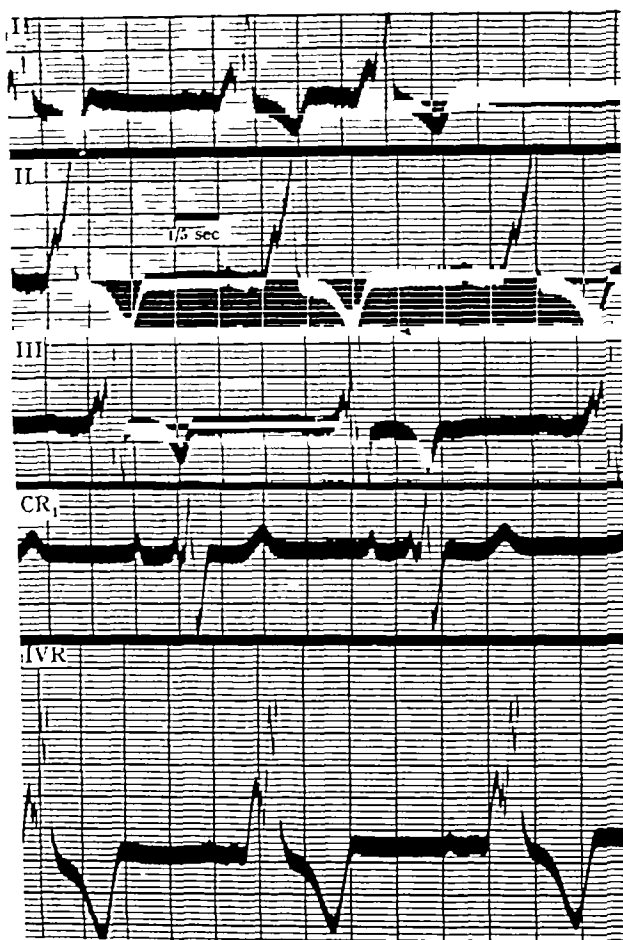
FIG 1 —Electrocardiogram from Case 1 Sinus rhythm with extrasystoles, exceptionally wide QRS complexes with four R waves showing in IVR and deep inversion of the T waves in many leads
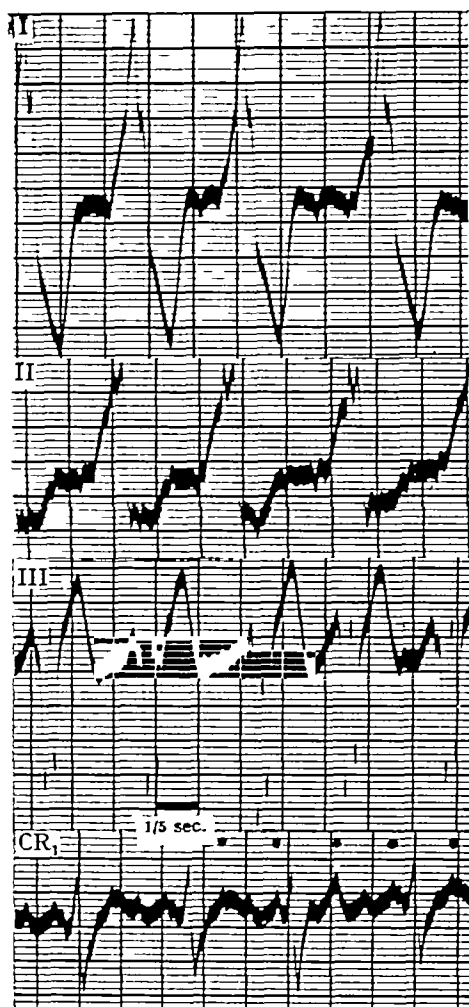
FIG 2 —Electrocardiogram from Case 1 Paroxysmal tachycardia with a high auricular rate and A-V dissociation.

tubercles with considerable focal fibrosis No tuberculosis found in lungs Central congestion of liver Chronic congestion and œdema of spleen, showing microscopically two miliary tubercles in pulp One old infarct in spleen and one in right kidney Congestion and severe post-mortem degeneration of kidneys Persistent glandular thymus No abnormality, macroscopic or microscopic in endocrine glands (Only one parathyroid identified) Post-mortem digestion of stomach No macroscopic or microscopic abnormality found in brain or spinal cord Middle ears normal Cyanosis of extremities No sub-

cutaneous œdema A well developed and well nourished young man

Weights Body, 62 5 kg (height, 1 7 m), heart, 1134 g , liver, 1921 g , kidneys, 333 g , spleen, 333 g , brain, 1495 g , suprarenals, 13 g , thyroid, 56 g , thymus, 20 g , testes, 21 g , pituitary, 0 6 g.

Microscopic examination Portions of the left ventricle and right auricle were fixed in Bouin's fixative The rest of the heart was fixed in formaldehyde, blocks being taken on the following day from both ventricles, interventricular septum, and sino-auricular node In addition to hæmatoxylin and
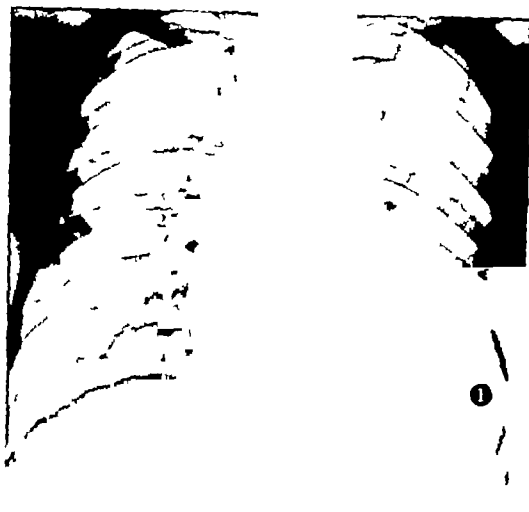
FIG 3—Teleradiogram from Case 1   Great enlargement of the heart and especially of the left ventricle (1), much pulmonary congestion (2)
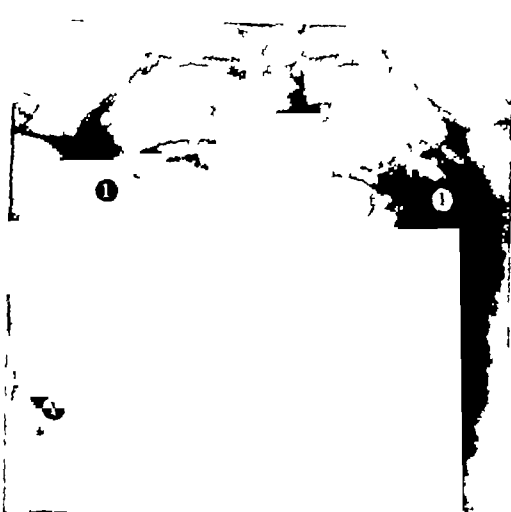
FIG 4—Teleradiogram from Case 1   Pulmonary œdema (1) is added to the great cardiac enlargement seen in Fig 3

eosin, iron hæmatoxylin and van Gieson and phosphotungstic-acid hæmatoxylin, sections from all blocks were stained by Best's carmine for glycogen   Frozen sections of a piece of left ventricle were stained with Sudan III for fat

Heart   In all parts examined there is dense patchy fibrosis of the myocardium, especially beneath the endocardium and pericardium, and gross hypertrophy of the muscle fibres (Fig 7)   The hypertrophy often appears greatest where there is most fibrosis   In ordinary stains the fibres are occasionally greatly vacuolated, but vacuolation in general is rather inconspicuous, except in phosphotungstic-acid hæmatoxylin preparations, where high magnifications frequently reveal clusters of small vacuoles in the centres of fibres, or groups of reddish-brown granules in a similar situation   In such fibres the longitudinal fibrils are restricted to the periphery of the muscle cell and cross-striation is lost   Cross-striation is preserved in many fibres devoid of vacuoles and granules   There is no fatty degeneration   The Bouin-fixed sections show conspicuous deposits of glycogen in many scattered fibres in both left ventricle and right auricle   There are no circumscribed areas in which all or most fibres are so affected, the change is diffuse   A good deal of finely granular material stained by Best's carmine is present in the intermuscular connective tissue and in the walls of capillaries   In the formalin-fixed tissue, however, there is little evidence of glycogen   The fibrous tissue in the myocardium contains few

spindle cells and occasional small lymphocytes which are mostly perivascular   Occasional larger clumps of small round cells appear to be due to submiliary granulomatous tubercles, one being identified with certainty in the interventricular septum, and one in the pericardium of the left ventricle   The pericardium elsewhere is little affected, there are a few small lymphocytes about the vessels, which are engorged   No changes were found in the special muscle fibres of the conducting system

Liver   In a block fixed in Bouin s fluid there is great congestion and atrophy of the centres of the lobules, in places adjacent atrophied areas are confluent   There is no fibrosis   A good deal of glycogen is present as fine cytoplasmic granules in the better preserved cells of the periportal parenchyma

Muscle   Portions of the tongue and vastus externus muscle were fixed in Bouin's fluid   In the tongue glycogen is restricted to the squamous epithelium and some cells of the mucous glands   In the vastus externus large quantities of glycogen are present, some being in the muscle fibres but most has escaped into the interstitial tissue   Patchy vacuolation of the fibres is demonstrated by other stains, but the degree of vacuolation appears trivial in comparison with the amount of glycogen   A special search for glycogen was made in Bouin fixed material from the kidney, spleen, and central nervous system with negative results

FIG 5—Photogram of the heart in Case 1 There is very great general hypertrophy and especially of the left ventricle (1) which shows grey patches of fibrosis (2)

Case 2 Male, aged 20 years His appearance was healthy and he complained of no symptoms when he was referred by a service medical board because of great outward displacement of the apex beat Later he admitted that during the past six months he had been compelled through giddiness to halt the omnibus he drove, but had never lost consciousness The pulse was normal in rate and irregular from auricular fibrillation The blood pressure was 125/80 The apex beat was near the left anterior axillary line and was forcible The heart sounds were clear and there were no murmurs Triple heart rhythm was present from addition of the third heart sound There was no enlargement of the liver, nor of the spleen, and on examination the other systems, including the nervous system, were normal The blood sugar and the blood cholesterol were both normal The electrocardiogram showed
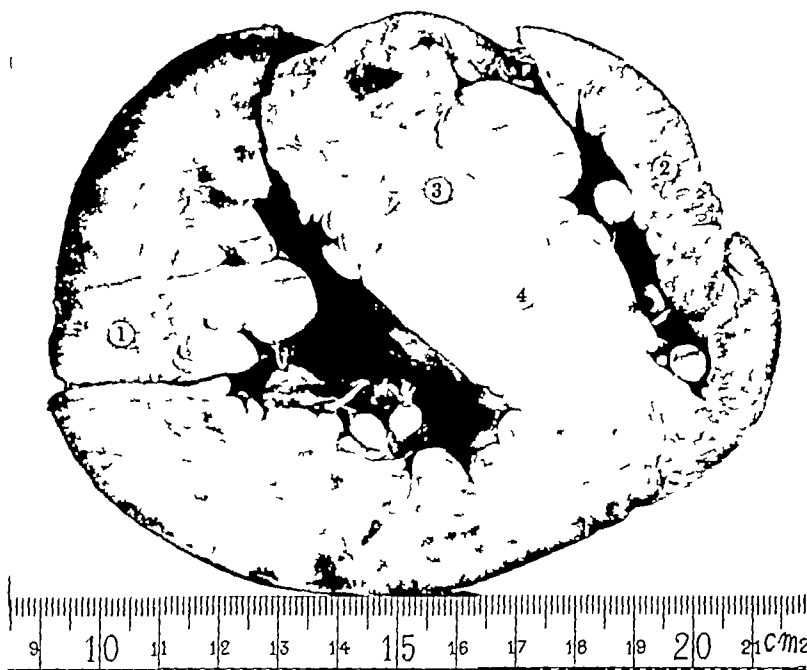
FIG 6 —Cross-cut of the heart in Case 1 to show great hypertrophy of the left
ventricle (1) right ventricle (2) and the septum (3), which shows extensive
fibrosis (4)
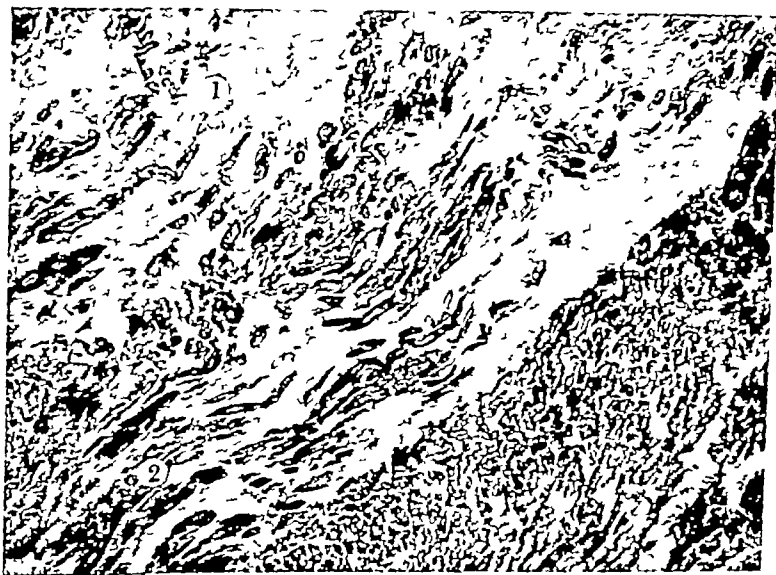
FIG 7 —Microscopical section of the myocardium from Case 1 showing great
fibrosis (1) and hypertrophy of surviving muscle fibres (2)
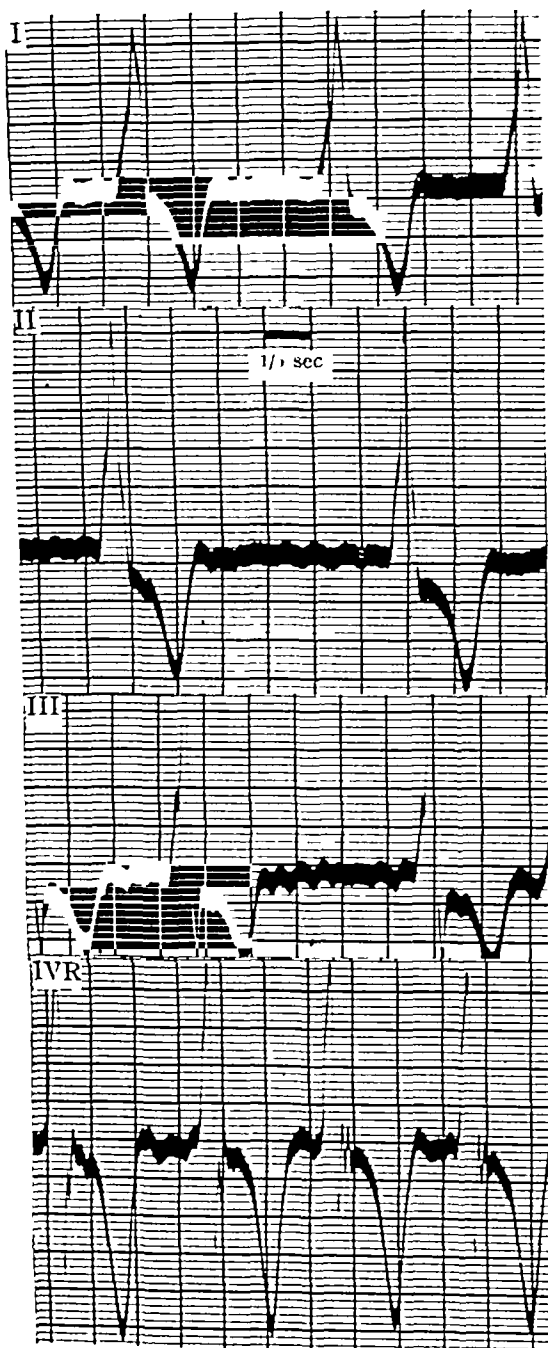
FIG 8 —Electrocardiogram from Case 2 Auricular fibrillation wide QRS complexes with deep inversion of the T waves in all leads
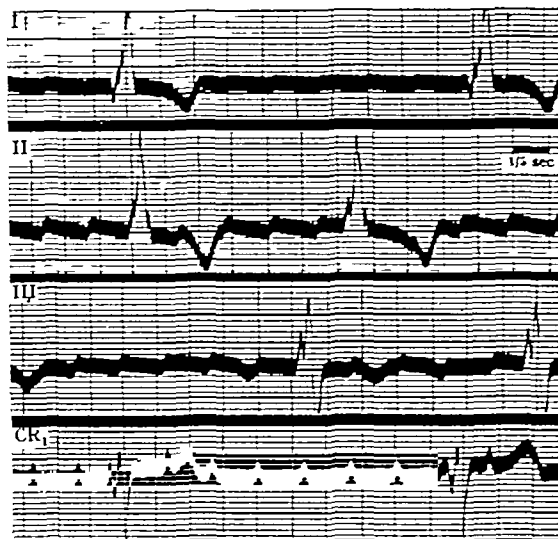
FIG 9 —Electrocardiogram from Case 2 Auricular flutter with slow ventricular rate Varying A-V dissociation
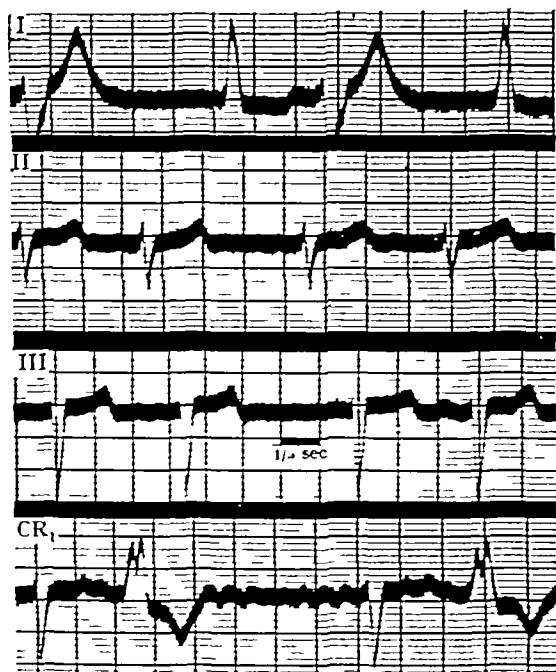
FIG 10 —Electrocardiogram from Case 3 Auricular fibrillation and extrasystoles the T wave is inverted in lead I, and the R wave is small in CR1

auricular fibrillation, exceptionally wide QRS complexes, and deeply inverted T waves (Fig 8) Another time (Fig 9) he showed auricular tachycardia with infrequent ventricular rate   On cardioscopy (Fig 11) there was great enlargement of the heart, and particularly of the left ventricle, the left border of which was remarkably quiet compared with the pulsatile right auricle at the opposite cardiac border

Case 3   Female, aged 43 years   For 12 years she had suffered from infrequent but severe syncopal attacks   Her pulse was about 70 a minute and was irregular from auricular fibrillation   The blood pressure was 130/90   The apex beat was displaced outwards and was forcible   The heart sounds were clear and there were no murmurs   There was conspicuous splitting of the second heart sound and this was confirmed by the phonocardiogram   There was no enlargement of the liver nor spleen, and examination of other systems showed no abnormal signs   There were extrasystoles and auricular fibrillation with inversion of the T I (Fig 10)   On cardioscopy (Fig 12) there was moderate enlargement of the heart, and especially of the left ventricle

These three patients illustrate the familial and hereditary nature of the illness, Cases 1 and 2 were brothers and were the sons of Case 3, whose husband and a third son, aged 17 years, were healthy, an infant son had died at the age of 18 months from " heart trouble ", her parents died at the ages of 34 and 35, but the manner of their deaths could not be ascertained, a brother and sister as well as their offspring were healthy, one sister died suddenly in a tramcar at the age of 26 although she was thought to be healthy up to that time, another sister died unexpectedly at the age of 30, a brother while on his way to work one morning dropped dead on the pavement at the age of 21, details of necropsy in these cases cannot be traced, but the manner of their deaths makes it likely that at least six members in two generations of the same family suffered from the condition that is described here (Fig 13)   A family history of the same illness was also obtained from a patient reported at the Massachusetts General Hospital (1942) and also in one described by Addarii and Mahaim (1946)

In addition to the three cases already described there were six others whose symptomatology and clinical signs were so similar as to make me believe that they suffered from the same condition   In one where a necropsy was carried out, fibrosis of the myocardium was found to be the underlying lesion as in Case 1, but no family history of the condition could be obtained from any of the six cases, although in none had it been possible to examine other members of the family

Fig 11 —Teleradiogram from Case 2 showing great general enlargement of the heart and especially of the left ventricle (1)

Fig 12 —Teleradiogram from Case 3 showing moderate general enlargement of the heart and especially of the left ventricle (1)
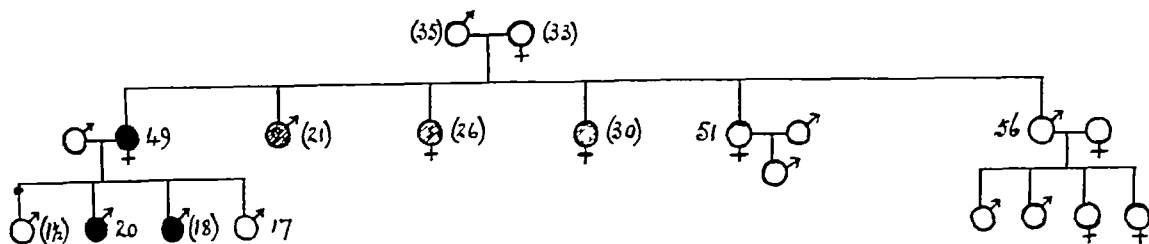
Fig 13 —Scheme identifying patients affected with Familial Cardiomegaly in one family   The black symbols represent members suffering from familial cardiomegaly, the shaded symbols indicate members probably affected by the same illness   the unshaded symbols are unaffected members   The numerals are the ages in years, and when bracketed they indicate the age at death

OTHER CASE NOTES

Case 4   Male, aged 35 years   Two years before he was rejected for military service by a medical board which advised him not to do any heavy work He remained well until a month before when he fainted in a chair and afterwards discovered a lump on the back of his head which he supposed had resulted from his head falling backward on to the chair   Thereafter he experienced spells of giddiness which made him uncertain of himself when walking, but when they passed he would feel quite well Only once did he lose consciousness   No other members of the family were similarly affected

His appearance was healthy   The pulse was slow (52 a minute), and was irregular from extrasystoles, which disappeared for a short time after exercise

The blood pressure was 115/70   The apex beat reached the anterior axillary line and was forcible in character with a double impulse   There was no thrill   A triple heart rhythm was present from the addition of the third heart sound and this was confirmed by the phonocardiograph   There were no murmurs   Further routine clinical examination showed no abnormal signs in other systems   The electrocardiogram (Fig 14) showed bradycardia, bundle branch block, and extrasystoles   On cardioscopy (Fig 16) there was great generalized enlargement of the heart   The Wassermann reaction was negative   He continued with his work, but complained of giddiness on occasions   Three years later there was another syncopal attack, but he recovered only to fall dead as he was walking home from work   There was no necropsy
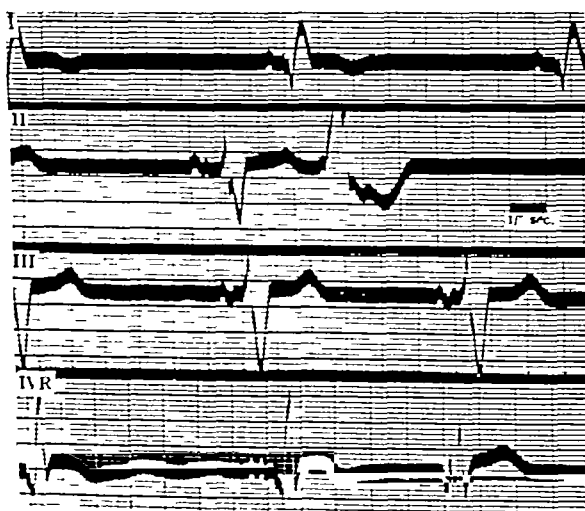
Fig 14 —Electrocardiogram from Case 4   Sinus bradycardia with extrasystoles   wide QRS complexes prominent Q R–T deviation, and inversion of the T wave in lead 1   Q wave and R–T deviation in IVR
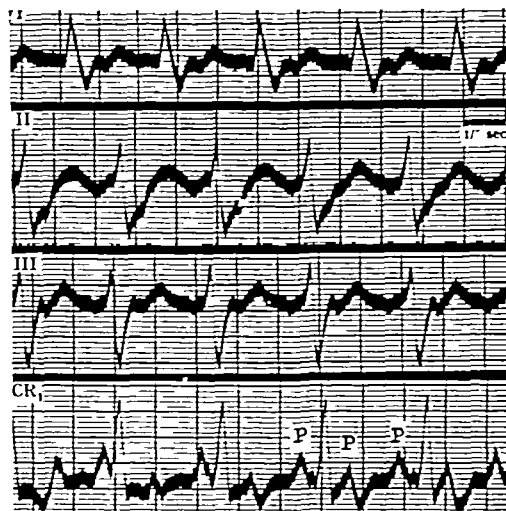
Fig 15 —Electrocardiogram from Case 5 during an attack of paroxysmal tachycardia with 2 to 1 A–V dissociation which is best seen in CR1

FIG 16 —Teleradiogram from Case 4 Great enlargement of the heart and especially of the left ventricle (1) pulmonary congestion (2)

Case 5 woman, aged 63 years Three years before, she complained of dizziness and at times lost consciousness Later, palpitation became troublesome and she said that the heart occasionally beat very rapidly The pulse was 56 and irregular from extrasystoles, and she was sometimes found with paroxysmal tachycardia There was no hypertension The apex beat was displaced outwards as far as the anterior axillary line and it was diffuse and forcible There was an obvious triple heart rhythm from addition of the third heart sound A systolic murmur in the mitral area occupied mid-systole and there were no diastolic murmurs Although the thyroid was enlarged, there were no signs of thyroid toxæmia There were no abnormal signs in any other system At one time sinus bradycardia with ventricular complexes of bundle branch block, and at other times paroxysmal tachycardia with 2 to 1 (Fig 15) or a higher grade A-V dissociation, were seen On cardioscopy (Fig 17) there was great enlargement of the heart, particularly of the right side She is still alive

Case 6 Woman, aged 62 years She was ad-

mitted to hospital for attacks of palpitation 15 years ago, although the arrhythmia did not recur in hospital, radiological examination showed enlargement of the heart. Throughout the years she continued to experience these attacks and in two of them she lost consciousness Two years ago an electrocardiogram showed sinus bradycardia and bundle branch block Twelve months ago a cardiogram during the attack showed auricular fibrillation and she again reverted to normal rhythm There were more episodes of paroxysmal auricular fibrillation, and unconsciousness once from cerebral embolism She gradually recovered from the paralysis and for three months she had not experienced any palpitation while the heart rhythm continued as auricular fibrillation with infrequent ventricular rate The cardiogram showed right bundle branch block in addition to fibrillation The blood pressure was normal The apex beat was out a little way and there was moderate cardiac enlargement No triple heart rhythm was present at the single clinical examination There was no enlargement of the liver or spleen and the urine was clear Since the auricular fibrillation became established the syncopal attacks had become less frequent

FIG 17—Teleradiogram from Case 5 There is enlargement of the left ventricle (1) and especially of the right auricle (2) Pulmonary congestion (3)

FIG 18—Teleradiogram from Case 7, showing enlargement of the heart and especially of the left ventricle (1)

FIG 19—Teleradiogram from Case 9 showing great enlargement of the heart and especially of the left ventricle (1) with pulmonary congestion (2)

FIG 20—Teleradiogram from Case 8 showing generalized enlargement of the heart and especially of the left ventricle (1) and right auricle (2), as well as pulmonary congestion (3)

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toxæmia There were no abnormal signs in any
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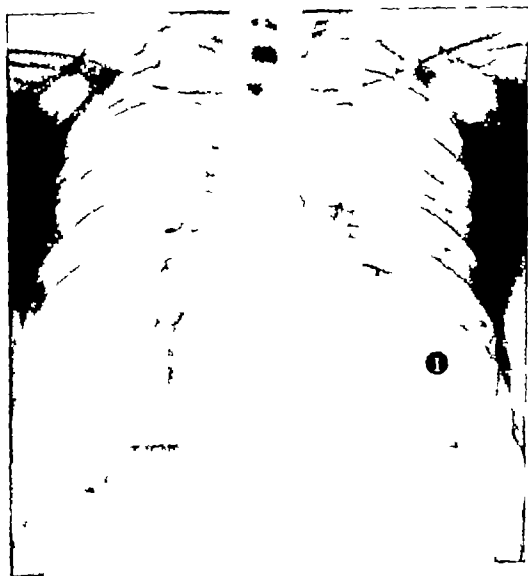
FIG 18—Teleradiogram from Case 7, showing enlargement of the heart and especially of the left ventricle (1)

FIG 19—Teleradiogram from Case 9, showing great enlargement of the heart and especially of the left ventricle (1) with pulmonary congestion (2)

FIG 20—Teleradiogram from Case 8 showing generalized enlargement of the heart and especially of the left ventricle (1) and right auricle (2), as well as pulmonary congestion (3)

FIG 21 —Microscopical section of the myocardium from Case 8 showing great fibrosis (1) and hypertrophy of surviving muscle fibres (2)

Case 7   Man, aged 41 years   Although he had complained of breathlessness on exertion for some years he had not sought medical advice, and enlargeme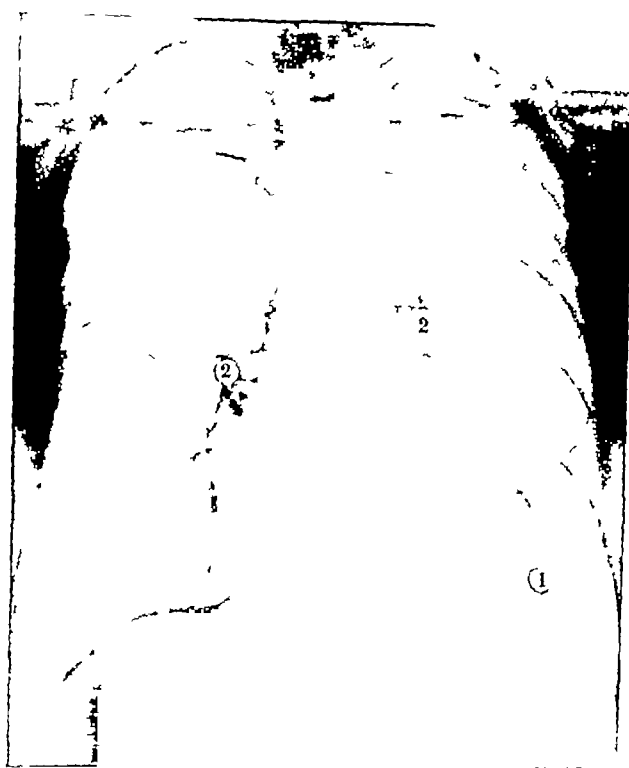nt of the heart was discovered on routine mass radiography   He had neither palpitation nor giddiness   No other members of the family complained of heart trouble, but none of them was examined

The pulse was regular and 76 a minute   The blood pressure was 120/85   The apex beat was in the left anterior axillary line   A systolic murmur was heard in late systole in the mitral area and there was prominent splitting of the second heart sound which was confirmed in the phonocardiogram There were no diastolic murmurs

There was no enlargement of the liver and no other abnormal physical signs   The urine was clear   The electrocardiogram showed bundle branch block   On cardioscopy (Fig 18) there was considerable enlargement of the heart especially involving the left ventricle, there was no pulmonary congestion

Case 8   Boy, aged 12 years   His mother said that for several months he had been subject to attacks of fainting   Three such attacks occurred in the previous fortnight   They had all taken place while he was at school   There was never any warning and he would fall down suddenly   In one attack he hurt his head badly when it banged against the floor   There were no other complaints, and the mother had been told he had epilepsy   There was no family history of a similar illness

The boy looked healthy   The pulse was rather slow (60 a minute) and was regular   The blood

pressure was low (105/50)   The apex beat was out a little way and he showed a short soft systolic murmur   There was triple heart rhythm   No other physical signs presented and there was no enlargement of the liver or spleen   The urine was clear The cardiogram (Fig 22) showed sinus rhythm at a slow rate (48 a minute) and a very high voltage The P–R period was not prolonged nor was the QRS period   There was deviation of the R–T segments, and the T waves were diphasic in certain leads   On cardioscopy (Fig 20) there was generalized enlargement of the heart and especially of the left ventricle

He continued to suffer from epileptiform attacks Four years later, at the age of 16, he developed acute appendicitis and recovered uneventfully from the operation   The day following his discharge from hospital while walking home from the cinema he was seized with severe breathlessness and died on his way to hospital

At necropsy there was considerable enlargement of the heart (weight not recorded), and particularly of the base of the left ventricle   There was no embolism and no abnormality of the coronary circulation   On microscopical examination there was great hypertrophy of the myocardial fibres of the left ventricle with much interstitial fibrosis (Fig 21)   (See appendix for mother's history)

Case 9   Man, aged 33 years   He was without symptoms apart from palpitation until three months before when he began to get breathless on exertion His voice had altered and this brought him to hospital where palsy of the left recurrent laryngeal nerve was found   The pulse was irregular from

extrasystoles and the nature of the arrhythmia was confirmed by the cardiogram (Fig 23) which also showed wide QRS complexes like those of bundle branch block The apex beat was displaced outwards as far as the left anterior axillary line and radiological examination confirmed the presence of great enlargement of the heart (Fig 19) The blood pressure was 120/75 The first heart sound showed splitting and there was a slight systolic murmur in the mitral area The house physician did not note that any triple heart rhythm was present There were no other abnormal signs The urine was clear The sugar tolerance test was normal and the Wassermann reaction was negative He left hospital without a definite diagnosis having been made He died a few months later but there was no necropsy

DISCUSSION

Unexplained cardiac enlargement is not common Now and again, however, there comes for diagnosis a patient in whom the cause of an enlarged heart is not obvious In older patients hypertension may explain cardiac hypertrophy, even though the blood pressure at the time is normal, perhaps reduced by cardiac infarction which can by itself cause a moderate or greater degree of cardiac enlargement In a younger patient such diagnosis will seldom apply Bradycardia, with or without heart block, will explain some instances of enlargement of the cardiac silhouette found on radiological examination An unusual condition like amyloidosis of the heart has been the cause of moderate enlargement in rare cases Enlargement of the heart from glycogenic disease is even a rarer event in adults Whenever a single example of unexplained enlargement of the heart is seen the need to find the precise cause has not appeared so important, but when two
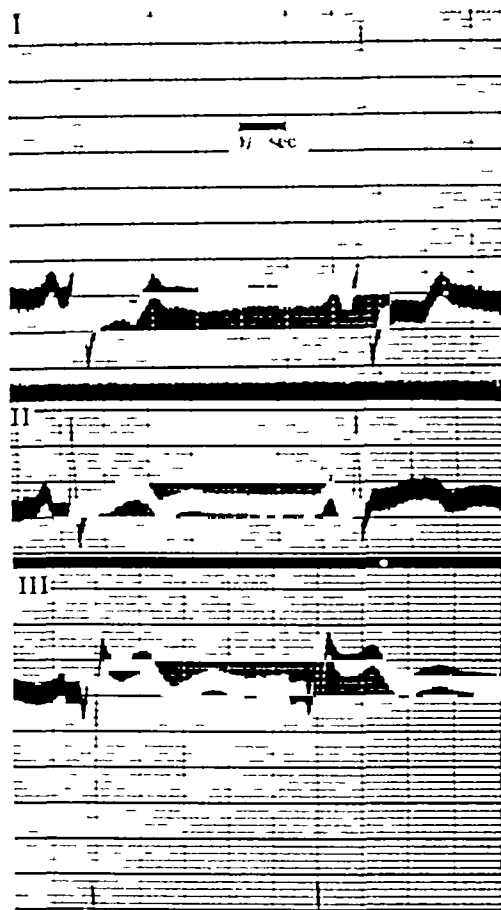
FIG 22 —Electrocardiogram from Case 8 showing sinus bradycardia deviation of the R–T segments and diphasic T waves
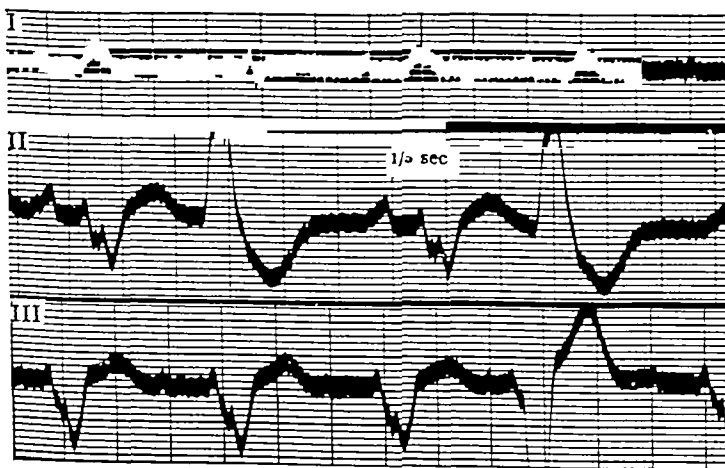
FIG 23 —Electrocardiogram from Case 9 showing left bundle branch block and extrasystoles

or more such cases appear, a search for a common aetiology becomes more vital

When the pathological findings have not been available or are equivocal in these odd instances of cardiac enlargement they have been described under such titles as ' idiopathic enlargement,' or ' unexplained enlargement of the heart in young subjects' (Whittle, 1929, Kugal and Stoloff, 1933, Levy and Rousselot, 1933, Mahon, 1939, Levy and von Glahn, 1937, Case Records of Massachusetts General Hospital, 1942, Norris and Pote, 1946, and Vulliamy, 1947)   When inflammatory changes or fibrosis of the myocardium has been an obvious finding at necropsy, they have appeared as acute non-specific myocarditis (Helwig and Wilhelmy, 1939, Candel and Wheelock, 1945), myocardial fibrosis in young men (Sellars and Phillips, 1946), and chronic fibroblastic myocarditis (Ware and Chapman, 1947)   Again, the pronounced degree of cardiac enlargement has sometimes been emphasized in a title such as massive cardiac hypertrophy (Doane and Skversky, 1944), while the arrhythmia which is common in such conditions has twice furnished the heading (Major and Wahl, 1932, Addarii, Mahaim, and Winston, 1946)   Few of the cases published under these several titles are instances of the condition described here

In the published cases of obscure cardiac enlargement the metabolism of glycogen has often been discussed   In Case 1 of the present series, deposits of glycogen appeared in many scattered muscle fibres in the left ventricle and the right auricle, and in the vastus externus muscle   Russell (1948) sought to control this finding from the examination of 11 cases at necropsy which took place from 4 to 34 hours after death, they showed scanty amounts of glycogen in the ordinary muscle fibres compared with that found in Case 1 which was examined 56 hours after death   Berlinger (1912) found little glycogen in 25 hearts beyond occasional traces in those cases where necropsy was delayed till five hours after death, the auricular appendage contained more glycogen than other parts   The work of Vallance-Owen (1948), however, has shown that post-mortem material does not appreciably lose its glycogen content up to 50 hours before fixation if kept in a cold chamber, this has corrected the customary belief that when glycogen is found in old post-mortem tissue, more would have been found had fixation of the tissue been carried out immediately after death   The small amount of glycogen found in the liver in Case 1 is without significance for Popper and Wozasak (1930) found glycogen in cases of heart failure   No glycogen was found in the kidney, spleen, or central nervous system in

Case 1   The patients described in this paper are not examples of glycogenic or von Gierke's disease (1929), a condition found in infants where glycogen accumulating in the liver, and rarely in the kidneys and the heart, causes the viscus to enlarge, and where biochemical tests establish a failure in glycogenolysis so that there is ketosis, hypoglycæmia, with absence of the normal rise in the blood sugar after adrenal line, and an abnormal blood sugar curve after glucose, together with a raised blood glycogen and blood cholesterol (Ellis and Payne, 1936)   Gardner and Simpson (1938) found 40 reported cases of glycogenic disease, but in none of them had death taken place suddenly or required a medico-legal examination   They recorded the first example of this, a boy aged 11 years   The age of this patient was also exceptional because in the ten previously recorded cases of glycogenic disease in which the presence of excessive glycogen had been demonstrated in the heart muscle, either by Best's stain or by chemical analysis, the ages ranged from 5 weeks to 8 months   Mason and Anderson (1941) have recommended that the term von Gierke's disease should be confined to cases in which there is failure of glycogenolysis   I agree with this view and would add a second criterion, namely, that the designation should be applied to the heart only when it has enlarged from accumulation of glycogen within it   If these rules are applied it is likely that the diagnosis needs to be considered in infants and only rarely in older children or adults

Of greater significance is the similarity of the signs met with in the present series to those found in Friedreich disease   The familial and hereditary nature of the illness in 3 out of 9 cases is comparable with a series of patients with Friedreich disease where 18 of 38 were the only members of their family to be affected   The heart is commonly affected in Friedreich disease for 12 out of 38 patients showed prominent electrocardiographic changes (Evans and Wright, 1942), such irregularities in the cardiogram told of an interruption of the conducting tissue with complete and bundle branch block, or of involvement of the myocardium producing inversion of the T waves reminiscent of cardiac infarction   Because of the lesser degree of myocardial fibrosis in Friedreich disease, the remarkable widening of the QRS complexes in some of the cases described in this paper, is not found   The size of the heart is not as great in Friedreich disease, but to this finding there are exceptions especially when heart block is present   On pathological grounds too the similarity of Friedreich disease to the condition dealt with here is arresting   Russell (1946), reporting specially on the heart in four cases of Friedreich

disease, found a piece-meal destruction of muscle fibres with fibrosis and hypertrophy of the surviving fibres, and remarkably little cellular inflammatory infiltration, there was no glycogen in one heart, but it was not sought specially in the other three Naturally, the relation of this condition to Friedreich disease would be more definitely established if instances of each were met with in one family, but such a coincidence has not so far come to my notice

SUMMARY

There is described in this paper a distinct syndrome having a definite clinical, cardiographic, and pathological pattern

Clinically it is characterized by light symptoms at the start, and is often found fortuitously in a young adult during routine examination preliminary to admission to military service or civilian occupation Ultimately, palpitation, momentary giddiness, and frank Stokes-Adams attacks may develop, and death may come suddenly during such episodes, or as the result of heart failure precipitated by the onset of paroxysmal tachycardia

On examination the pulse is usually irregular from extrasystoles, paroxysmal tachycardia, auricular fibrillation, or heart block There is great enlargement of the heart, and the blood pressure is normal The heart sounds are usually clear, and there is either splitting of the second sound, or triple heart rhythm from the addition of the third heart sound There is no enlargement of the viscera, and serological tests and the blood chemistry are normal

The *electrocardiogram* shows extrasystoles, paroxysmal tachycardia, auricular fibrillation, or heart block, according to the kind of arrhythmia prevailing at the time, the QRS complexes are usually exceptionally wide, depending on the extent of the fibrosis and the size of the heart, and the T waves are inverted

On *cardioscopy* there is enlargement of the heart, and as a rule the cardiomegaly is considerable

The *prognosis* depends on the extent of the fibrosis and the associated cardiac enlargement Thus, it is poor in young subjects with great enlargement of the heart, but in older subjects with moderate cardiac enlargement the outlook can be favourable although recurrent Stokes-Adams attacks are a handicap if frequent

Pathologically the condition shows fibrosis of the myocardium is usually conspicuous, this is associated with hypertrophy of the remaining muscle fibres producing great cardiac enlargement Intracardiac thrombosis initiating embolism is an

H

expected complication Although glycogen may be present and even in slight excess of the normal, the syndrome described here should be regarded as a separate entity from glycogenic or von Gierke's disease—is usually confined to young children or infants—where a viscus becomes distended by the large accumulation of glycogen within it, and where laboratory tests during life show faulty glycogenolysis Neither does the syndrome include those cases of hypertrophy of muscle fibres in the absence of myocardial fibrosis

The *aetiology* of the condition, although obscure, probably rests with an unknown factor which in Friedreich disease involves the central nervous system alone or along with the heart, and in the condition described here affects the heart exclusively, causing myocardial fibrosis Like Friedreich disease too the condition may be familial and hereditary, or it may arise sporadically and *de novo*

Having regard to the specificity of the condition and its chief characteristics I propose to name it *Familial Cardiomegaly*

APPENDIX

Since this paper was written the mother of Case 8 has been admitted to hospital She is 42 years of age and for two months has experienced short attacks of paroxysmal tachycardia Once she lost consciousness for six minutes Her pulse is regular and the blood pressure normal The apex beat is in the left anterior axillary line There are no murmurs A triple heart rhythm from addition of the fourth heart sound is caused by delayed A-V conduction and there is splitting of the second sound in the mitral area from bundle branch block, these findings have been confirmed by the phonocardiograph The electrocardiogram shows a prolonged P-R period and bundle branch block On cardioscopy there is considerable generalized enlargement of the heart and much pulmonary congestion She is, therefore, another example of familial cardiomegaly, her son, Case 8, having died suddenly at the age of 16 from the same condition The addition of this patient to Cases 1, 2, 3, and 8 supplies five instances of the disease where a family history of the complaint was present

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THE EFFECT OF DIGITALIS ON THE VENOUS PRESSURE

BY

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The action of digitalis on the circulation in man is not yet clearly understood There can be no doubt that it benefits most patients with congestive heart failure, but beyond this there is no certainty

McKenzie (1905) believed that its value was greatest in cases of congestive heart failure with auricular fibrillation and could then be attributed to slowing of the ventricular rate, Lewis (1937) agreed maintaining that improvement was infrequent in patients with normal rhythm, because slowing of the heart rate was often inconspicuous Dock and Tainter (1930) and Katz et al (1938) suggested that digitalis might act primarily by constricting the hepatic vein, a throttle mechanism that was demonstrated in anæsthetized dogs, they claimed that the venous pressure was lowered by means of a bloodless venesection, blood being dammed back in the liver and portal system Such a theory harmonized with other findings, e g. digitalis reduced the cardiac output of normal dogs (Harrison and Leonard, 1926) and decreased the size of the heart in normal human beings (Stewart et al, 1938) In 1940, however, one of us was able to show that digitalis lowered the venous pressure in 90 per cent of cases of heart failure with normal rhythm, and that this was due neither to slowing of the heart rate nor to any hepatic vein throttle mechanism, for the venous pressure fell as sharply when cardiac slowing was prevented, and the liver and spleen shrank simultaneously (Wood, 1940) More recently, McMichael and Sharpey-Schafer (1944) showed that mechanical lowering of the right auricular pressure by means of cuffs on the thighs produced effects on the cardiac output in man similar to those resulting from digitalis in cases of congestive heart failure the right auricular pressure fell and the cardiac output rose, in normal subjects the right auricular pressure fell and the cardiac output fell They suggested that digitalis might have a primary action in lowering venous pressure to which the other effects were subsidiary The authors admitted that the venous pressure was lowered but slightly in normal subjects, and conspicuously only when the initial level was high, but they attributed this to a logarithmic effect

The object of the present investigation was to discover what action digitalis might have on the venous pressure when it was elevated from causes other than congestive heart failure

METHOD USED

A consecutive series of twelve cases, in which the jugular venous pressure was raised clinically without any real evidence of congestive heart failure, was studied The nature of the material is shown in Table I The raised venous pressure was attributed to a hyperkinetic circulatory state in the cases of anæmia and thyrotoxicosis, and to an increased blood volume in the cases of acute nephritis and artificial hydræmia Hydræmia was induced by means of sodium chloride 10 g, water 10–12 pints, and D O C A (desoxy-cortico-sterone acetate) 25–50 mg daily for 7 to 14 days

All observations were made with the subject lying more or less horizontal, the head being supported on one or two pillows The antecubital venous pressure was measured directly as described in a previous paper (Wood, 1940) The right auricular pressure was measured by means of a No 8, 9, or 10 nylon cardiac catheter and a saline manometer, as described by McMichael and Sharpey-Schafer (1944), only mean pressures can be recorded by this method The cardiac output was estimated by means of Fick's formula, the arteriovenous oxygen difference being obtained by analysing arterial and right auricular blood samples in a modified Haldane blood gas apparatus, and the oxygen consumption

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TABLE I

Case	Condition	Right ventricular pressure, cm saline above sternal angle at 5–10°	Oxygen consumption, ml a minute	Oxygen capacity, ml a litre	Arterio venous oxygen difference, ml a litre	Right auricular pressure (or antecubital venous pressure *) cm saline above sternal angle at 5–10° Before dig	After dig	Cardiac output, litres/minute Before dig	After dig	Blood pressure Before dig	After dig	Pulse rate Before dig	After dig
1	Pernicious anaemia	—	—			8 5*	8 5*						
2	Pernicious anaemia	24	382	48	28 6–37 6	1 5	1 0	10 5	10 0	132/60	140/60	112	108
3	Pernicious anaemia	13 5	262	88 5	34–32	–4 5	–4 5	7 4	8 2	120/66	128/66	94	90
4	Thyrotoxicosis and hypochromic anaemia	37	380	115	31–39	5 5	5 5	12 6	9 0	205/100	205/100	130	102
5	Thyrotoxicosis and aortic incompetence	—	257	169	46 5–51 5	–0 5	±0	9 7	5 6	120/40	165/80	90	58
6	Acute nephritis	20			59–61	7 5	7 0	5 6	4 4	138/78		65	
7	Acute episode in chronic nephritis		186	169	45–42 5	2 5	2 5	4 1	1 8	175/115	210/125	70	70
8	? Acute nephritis	15				4 0	4 0	1 95		130/80	155/85	72	48
9	Artificial hydraemia	11			105–115	16 0*	16 0*	6 4	6 5	100/60	110/64	84	76–80
10	Artificial hydraemia	14	208		41–40	–2 0	–0 5			160/100	170/100	96	96
11	Artificial hydraemia	—	260	161 Assumed normal		–1 0	–2 0						
12	Chronic constrictive pericarditis	10 5	286	Assumed normal	48–53	4 5	4 5	5 6	5 5	115/70	125/85	80	68–76

by means of a Benedict-Roth spirometer In some cases the arterial blood was assumed to be 95 per cent saturated with oxygen The oxygen capacity was either estimated directly by the ferricyanide method or calculated from the hæmoglobin value, results approximating closely when both methods were employed The catheter was passed without X-ray control to make certain the tip was in the right auricle, the right ventricle was always entered, and the catheter was then withdrawn slowly until the pressure suddenly fell and conspicuous pulsation ceased

RESULTS

Congestive Heart Failure In four controls with clinical congestive heart failure, mostly hypertensives, the venous or right auricular pressure fell sharply and considerably within half an hour of giving 1 5 mg of digoxin intravenously, whether initial readings were high or relatively low (Fig 1) At the same time the cardiac output rose, the pulse usually slowed, and the blood pressure rose (Fig 2) These cases illustrated the well-known response of heart failure to digitalis and proved that the

digoxin was potent and that the dose of 1 5 mg was sufficient

Anæmia There were three cases of severe pernicious anæmia in all the jugular venous pressures were raised as judged clinically The cardiac output was 10–14 litres a minute in one of them, 7 litres a minute in another, and was not measured in the third Intravenous digoxin had no effect on the venous or right auricular pressures and did not alter the cardiac output, the blood pressure, however, rose (Fig 3)

Thyrotoxicosis There were two cases of thyrotoxicosis in which the jugular venous pressures were raised as judged clinically one was complicated by moderate hypochromic anæmia, the other by atherosclerotic aortic incompetence The cardiac output was 12 litres a minute in the first, 9 6 in the second Intravenous digoxin had no effect on the right auricular pressure in either, the cardiac output fell appreciably in one of them, but this could be attributed to slowing of the pulse rate (Fig 4)

Acute Nephritis There was one case of classical acute nephritis, one of chronic nephritis with an acute flare-up, and one in which the diagnosis was
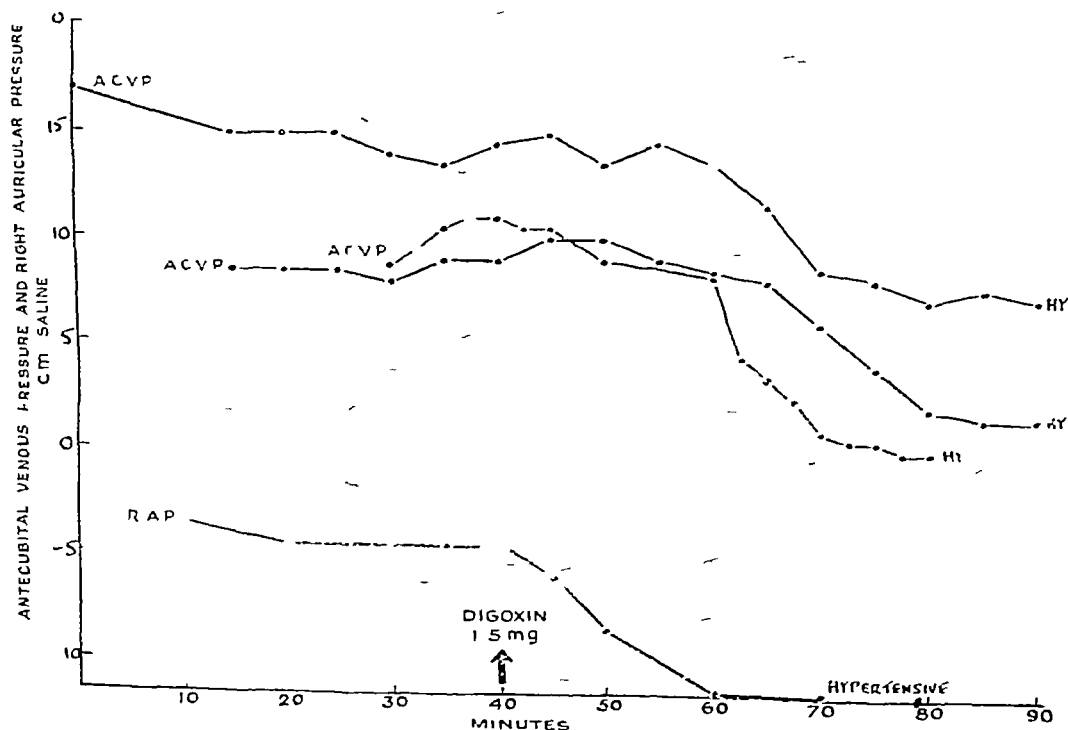
FIG 1 —Congestive heart failure The effect of intravenous digoxin on the venous or right auricular pressure in four cases of congestive heart failure with normal rhythm
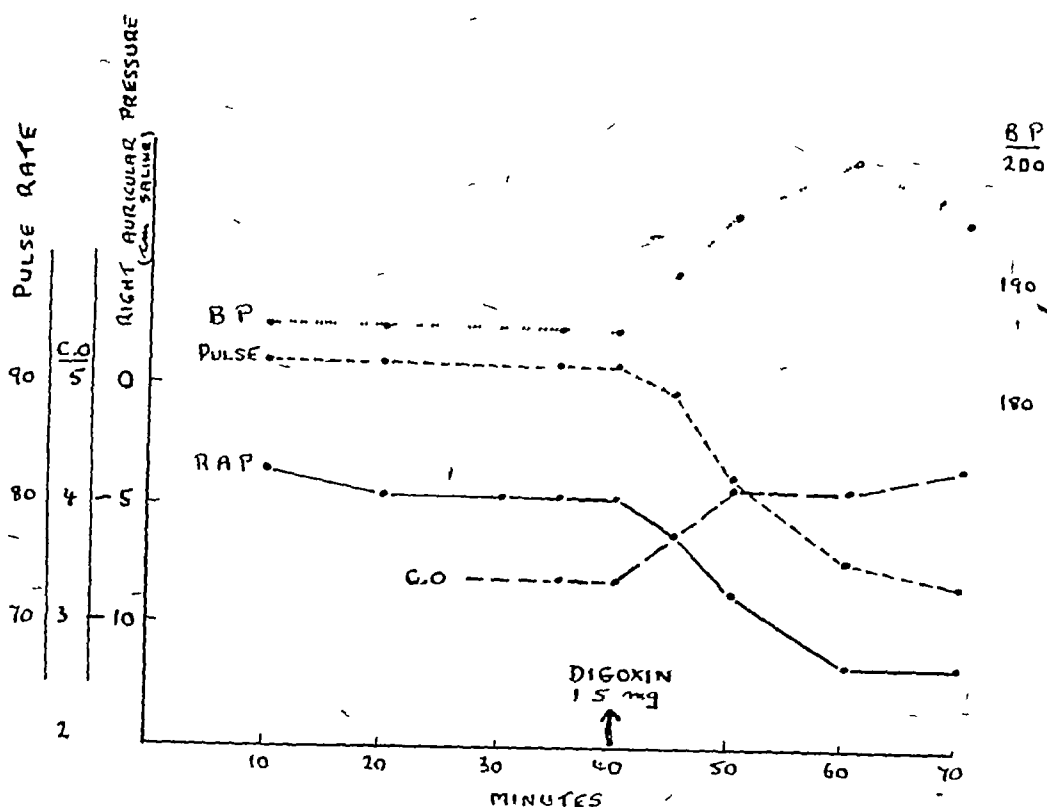
FIG 2 —Hypertensive heart failure The effects of intravenous digoxin on the blood pressure pulse rate, right auricular pressure and cardiac output in a case of hypertensive heart failure Oxygen capacity and hæmoglobin assumed normal Oxygen consumption assumed 300 ml /min A-V difference 87–68 ml /litre Right ventricular pressure +26 cm saline After rest, low sodium and mersalyl for 14 days

uncertain, this was a case in which transient œdema suddenly developed a fortnight or so after an acute upper respiratory tract infection, but the blood pressure, urine, and measured renal function remained normal All three had a raised jugular venous pressure

Intravenous digoxin (1.5 mg) did not influence the right auricular pressure or cardiac output in any of them, but the blood pressure rose as usual, and the pulse rate tended to fall (Fig 5)

Artificial Hydræmia Considerable increase in body weight, generalized œdema, and a raised jugular venous pressure were produced in three cases by means of salt, water, and desoxy-corticosterone Intravenous digoxin (1 5 mg) did not effect the right auricular pressure or the cardiac output in two of them, nor the venous pressure in the third (which was not catheterized) The blood

pressure rose and the pulse rate fell slightly in the case illustrated (Fig 6, see p 90)

Chronic Constrictive Pericarditis Only one case of Pick s disease was investigated, and the opportunity to catheterize a case of pericardial effusion did not arise Intravenous digoxin (1 5 mg) caused a rise in blood pressure and a fall in pulse rate, but had no influence on the right auricular pressure The cardiac output was not measured when the pulse reached its lowest level, but was not altered 10 and 40 minutes after the injection when the pulse rate was still unchanged or had practically regained its former level respectively (Fig 7, see p 91)

SUMMARY OF RESULTS

Digoxin thus had no effect on the right auricular pressure in these twelve cases (Fig 8) The blood
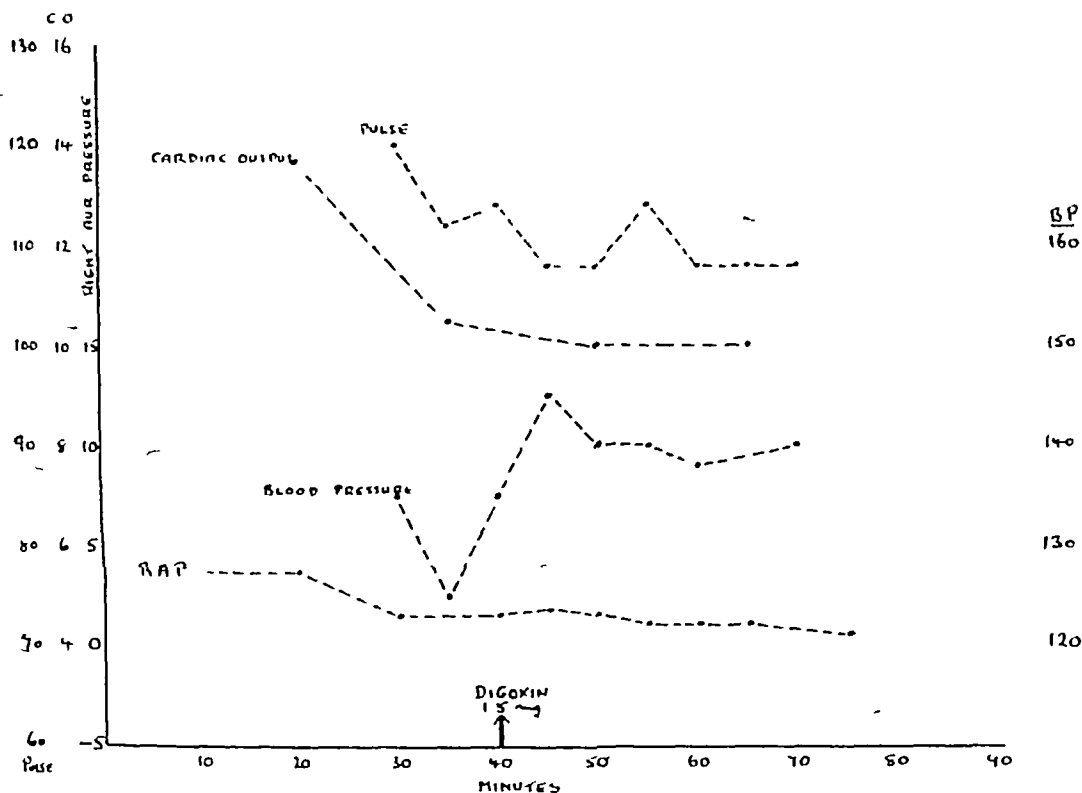
FIG 3 —Pernicious anæmia   The effect of intravenous digoxin in a case of pernicious anæmia   The cardiac output has fallen with the pulse rate, but there is no effect on the right auricular pressure   Oxygen capacity 4 8 vol per cent   Hæmoglobin 3 6 g per 100 ml (21 per cent Sahli)   Early oxygen consumption 390, late oxygen consumption 374   R V P   24 cm   saline A-V difference 28 6–37 6 ml /litre

pressure usually rose, and the pulse rate tended to fall, the cardiac output also fell if the pulse rate diminished sufficiently

The cases were selected at random and represented any condition that was encountered by the authors during 1947 and 1948 in which a raised jugular venous pressure could be attributed to causes other than congestive heart failure, moreover, they were consecutive, and no such cases have been excluded

Absence of congestive heart failure was confirmed by the behaviour of the cardiac output and by the arteriovenous oxygen difference   The former was high or normal, except in one (Case 10) complicated by nausea and vomiting, it fell with rest and slowing of the pulse, and was certainly capable of being raised considerably in some cases, if not in all   The latter was normal or less than normal, and was never increased (except in Case 10)   In congestive heart failure proper the cardiac output is low, or if it is normal or raised it is not as high as it should be,

in other words the circulation is incapable of meeting the demands of the body, the most consistent finding being an increased arteriovenous oxygen difference (Stead, Warren, and Brannon, 1948)

If digitalis had a primary action in lowering venous pressure it is difficult to believe that it would only influence the right auricular pressure in cases of congestive heart failure   The dose used, 1 5 mg of digoxin intravenously, was the same as that employed by McMichael and Sharpey-Schafer (1944), was sufficient to raise the blood pressure and slow the pulse rate in most cases, and had the usual effect in heart failure   Nevertheless, it is admitted that a larger dose might possibly be required in the type of cases investigated in this paper

If digitalis does not have a primary action in lowering venous pressure, its apparent ill effect in cases of chronic pulmonary heart failure secondary to emphysema (Howarth, McMichael, and Sharpey-Schafer, 1948) should be reviewed
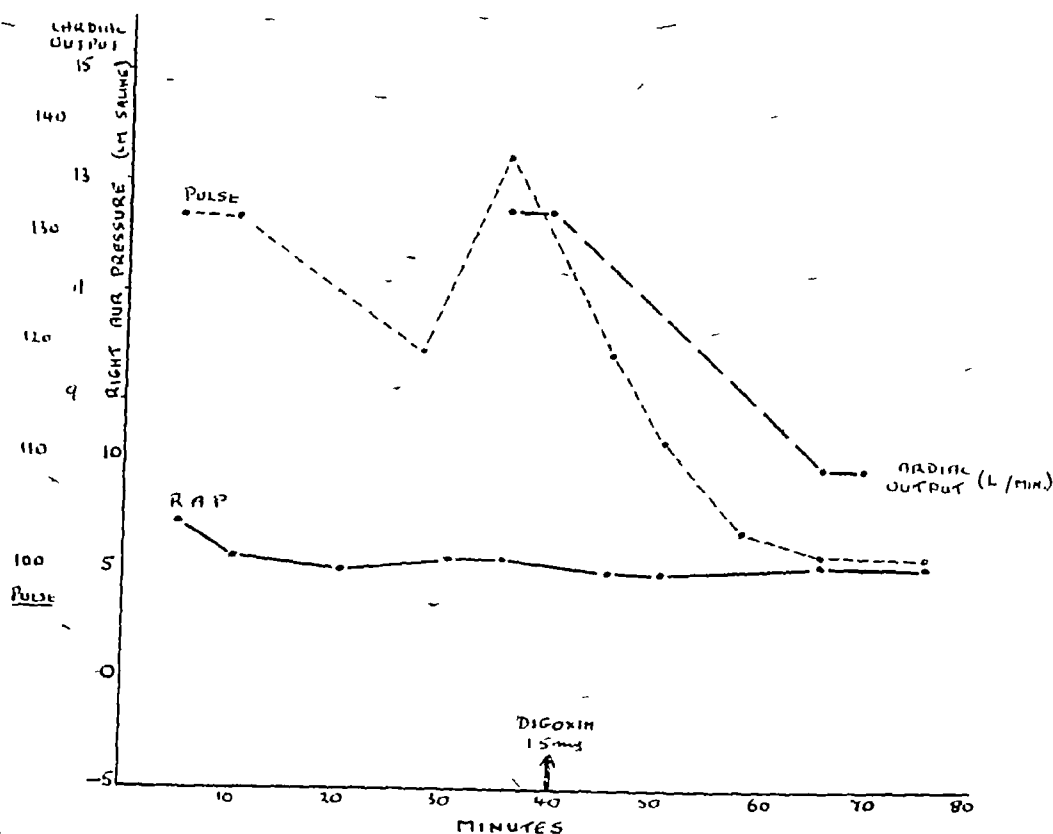
FIG 4 —Thyrotoxicosis and anæmia   The effect of intravenous digoxin in a case of thyrotoxicosis and anæmia   The fall in cardiac output parallels the fall in pulse rate, but there is no change in the right auricular pressure   B P   205/100/50 throughout   Oxygen capacity 11 5 vol per cent   Hæmoglobin 8 6 g. per 100 ml   Oxygen consumption 380 ml /min   R.V P   37 cm saline   A-V difference 31–39 ml /litre

SUMMARY AND CONCLUSIONS

The effect of digoxin on the venous pressure or right auricular pressure was investigated in four, cases of classical congestive heart failure with normal rhythm and in twelve cases in which the venous pressure was raised for other reasons   These cases included anæmia, thyrotoxicosis, acute nephritis, artificial hydræmia, and chronic constrictive pericarditis   The dose of digoxin was 1 5 mg intravenously in all instances

In the four examples of congestive heart failure the venous pressure or right auricular pressure fell conspicuously within 30 minutes, and the cardiac output, when measured, rose.

In the twelve patients without congestive heart failure the right auricular pressure did not alter appreciably within 40 minutes   The cardiac output, when measured, was either unchanged or fell with the pulse rate

A conspicuous pressor effect was demonstrated in most cases

It is concluded that intravenous digoxin, in doses of 1 5 mg intravenously, does not primarily lower the venous pressure, at least in the type of case described

As a corollary, it is suggested that the effect of digoxin on the venous pressure in cases of congestive heart failure may yet depend upon its direct action on the heart, as originally believed

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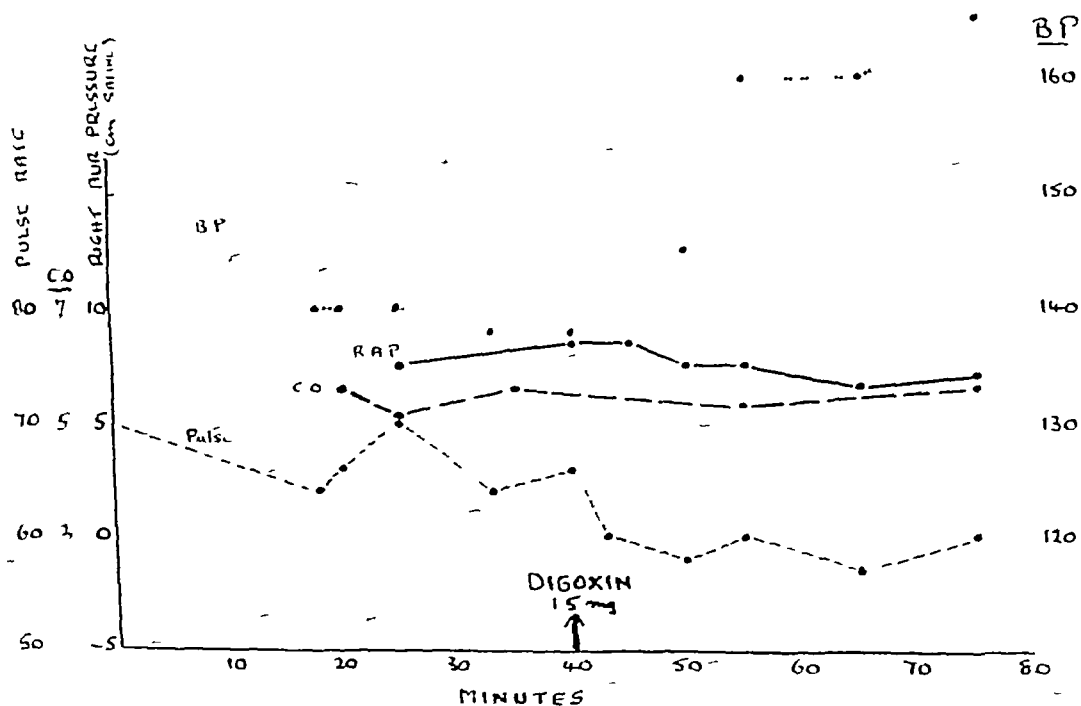
FIG 5 —Acute nephritis The effect of intravenous digoxin in a case of acute nephritis   There is no significant change in cardiac output or right auricular pressure, but there is a conspicuous rise of blood pressure Oxygen capacity 16 9 vol per cent Hæmoglobin 12 6 g per 100 ml Oxygen consumption 257 ml /min R V P 20 cm saline A-V difference 46 5–51 5 ml /litre
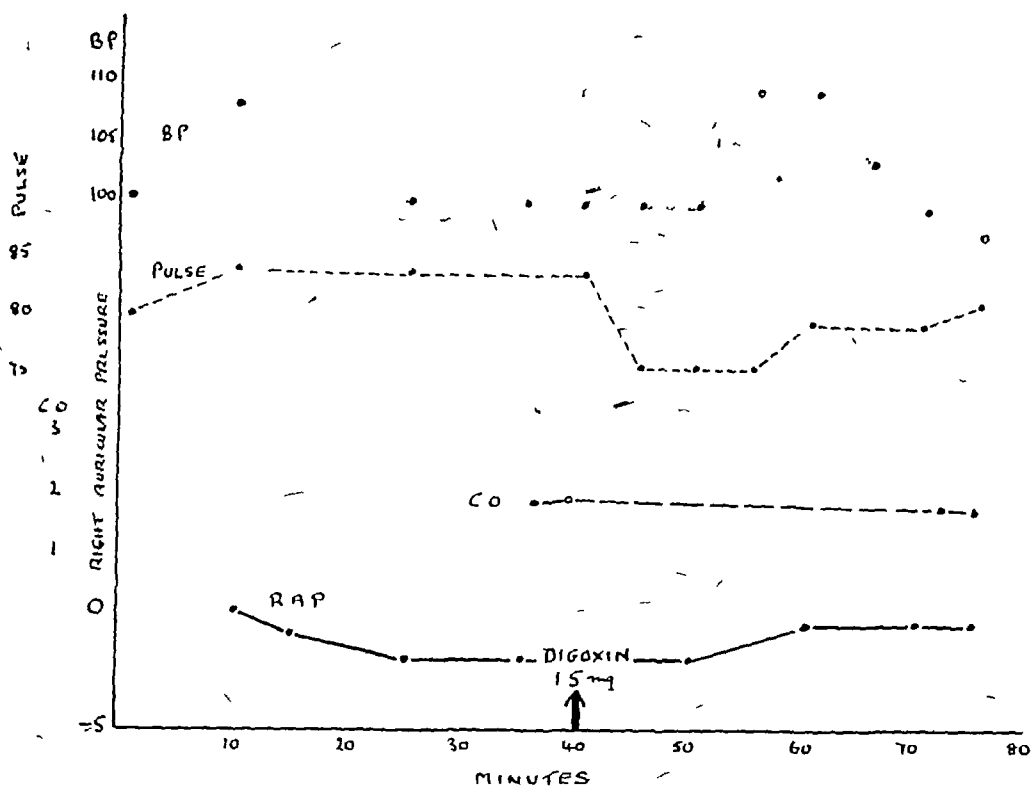
FIG 6—Induced hydræmia   The effect of intravenous digoxin in a case of induced hydræmia.   There is no change in the right auricular pressure   The usual pressor and slowing effects may be noted   Basal oxygen uptake 208 ml /min   Oxygen capacity 161 ml /litre   Hæmoglobin 12 g per 100 ml   R.V.P 14 cm saline   P A P 24 cm saline   A-V difference 105–115 ml /litre   Fourteen days preparation NaCl 10 g daily   Water 10–12 pints   DOCA 25–50 mg   Gained 11 lb   Œdema+J V P +2-3 at 35° Some nausea and vomiting

Fig 7 and 8   See next page
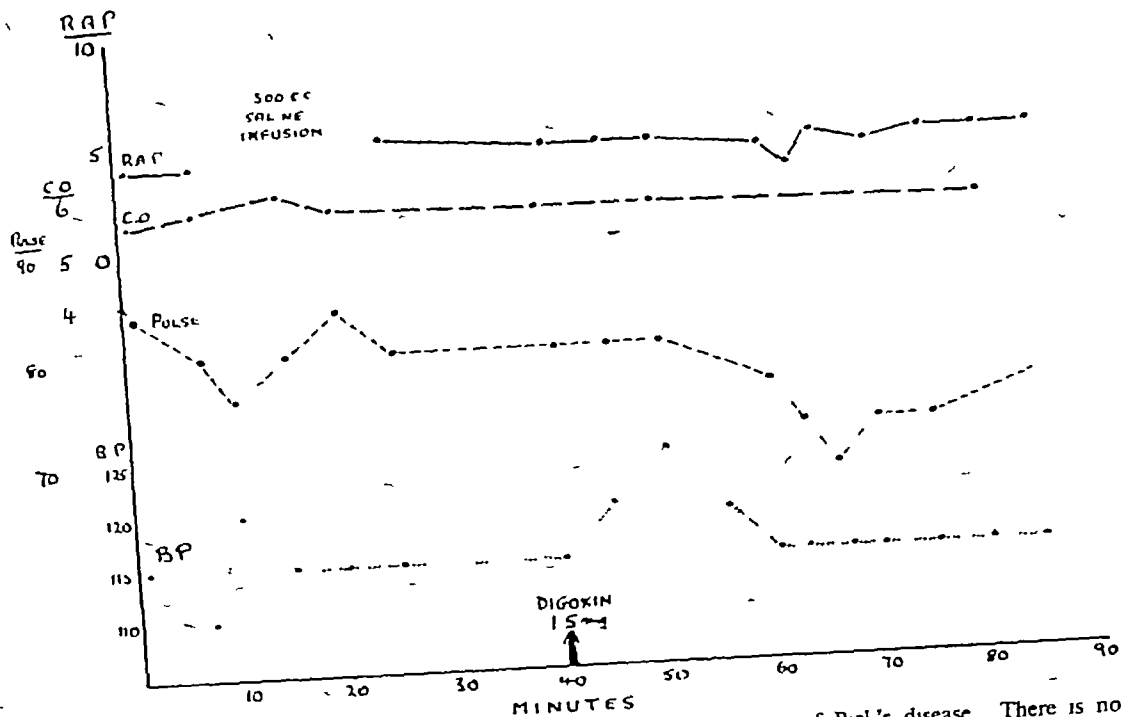
FIG 7—Pick's disease   The effect of intravenous digoxin in a case of Pick's disease   There is no change in the right auricular pressure   Oxygen consumption 286 ml /min   R V P 10 5 cm saline   Oxygen capacity assumed 20 vol per cent   A-V difference 48–54 ml /litre
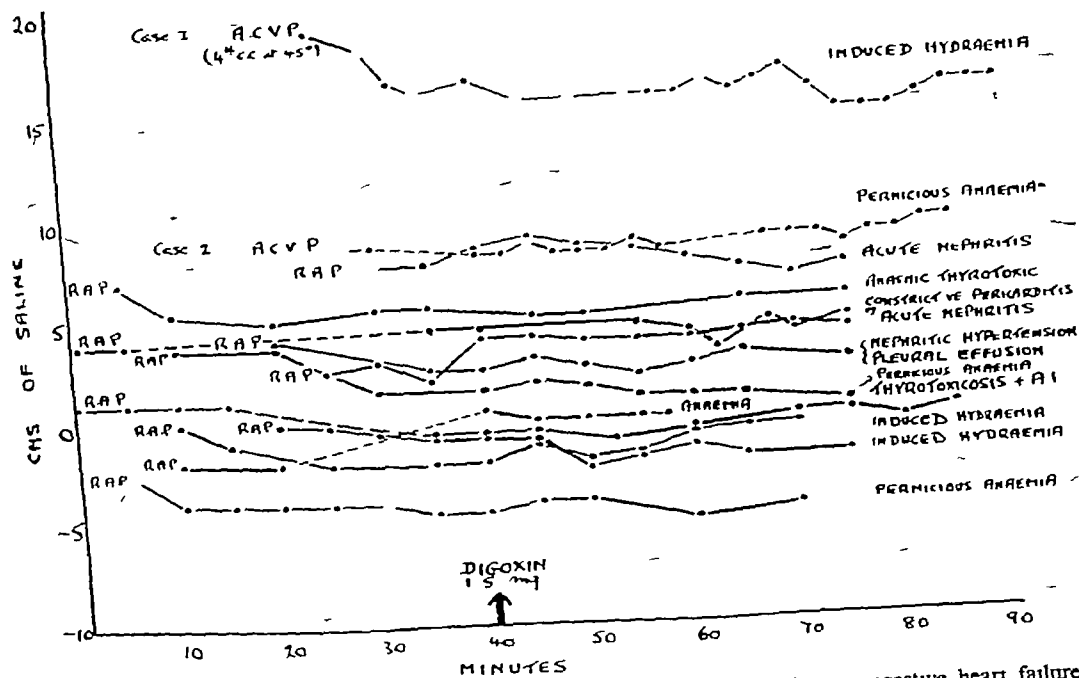
FIG 8—Absence of effect of digoxin on the venous pressure in cases without congestive heart failure   Superimposed charts illustrating the absence of appreciable change in the right auricular pressure as a result of digoxin in 12 cases characterized by a rise in venous pressure without heart failure

PROCEEDINGS OF THE BRITISH CARDIAC SOCIETY

A special AUTUMN MEETING of the BRITISH-CARDIAC SOCIETY was held at the Royal Society of Medicine, London on October 29, 1948 Chairman JOHN HAY The Chairman took the chair at 9 30 a m , 89 members and 38 visitors were present

CHEST LEADS

TERENCE EAST moved the adoption of the report that had been prepared by Curtis Bain, I G W Hill, Paul Wood and himself at the request of the Council (see page 103)

The following members then took part in the discussion

WILLIAM EVANS Since the introduction into this country of unipolar chest leads they had been accepted as ideal on theoretical grounds Doubtless in time things would sort themselves out, but in the meantime we must decide what helped us most when a patient with cardiac pain came to us for diagnosis Leatham had made a valuable contribution to this subject and we could see more clearly what we should do in the future , The following points which had been the main outcome of this study and of the application of the three chest leads, CR, CF, and V, in actual practice

(1) Since the T wave was so often inverted in CF leads in health, this lead should be discarded (2) CR1 depicted the P waves better than did V1, and for this reason it was a better lead to use in arrhythmia   (3) Since the R wave was better portrayed in CR1 than in V1, it proved a better lead for the diagnosis of septal infarction (4) Since the T wave was so often inverted in V1 in healthy adults, CR1 was a better lead to use in the diagnosis of right heart preponderance, for the T wave was seldom inverted in this lead in healthy adults (5) Again, since the T wave in V leads was usually small at the chest stations 6 and 7, sometimes becoming flat or inverted in health, the CR lead was superior in that the T wave in CR7 was always upright in health

For these reasons anyone who customarily used CR leads need not change to unipolar chest leads in the hope that they would gain additional information in clinical diagnosis, for they would be disappointed

PAUL WOOD A discussion on which chest leads are the best is not profitable, because they are all facets of the same thing thus conclusions drawn after comparing CR, CF, and V leads are obvious if unipolar limb leads have been taken with any chest lead The time had surely come to adopt unipolar leads in general.

The question of how best to mount the records might be trivial, but it seemed to be a problem that needed solution The obvious way was to mount the chest leads around a diagrammatic section of the heart in the positions from which they were actually taken, and to set Einthoven's triangle about them, the unipolar limb leads appearing at the apices and the standard leads along the sides This, however, was admittedly impracticable The next step was to make a more schematic diagram of the heart in the centre of the triangle, so that the chest leads appeared in a horizontal straight line This was also too laborious The diagram of the heart could be omitted with advantage, the leads being placed as before with reference to Einthoven's triangle Finally, the triangle could be dropped, and lead VF brought into line between leads II and III The result was neat, and the individual leads could be easily picked out according to their geographical relationship to an imaginary Einthoven's triangle Figures illustrating these suggestions were shown

K D WILKINSON Being old, I am not yet convinced that multiple electrocardiographic leads offer us greater security in the diagnosis of coronary occlusion These leads, if taken, should be recorded in the simplest possible form, and it seems to me that we shall only reach a definite conclusion when, by combination, we have records of a large number of cases complete with electrocardiograms and the findings of autopsies In the meantime, I want to stress the importance of taking a good history in every case

MORGAN JONES It is not claimed that the "unipolar" limb leads are precisely unipolar, so it is perhaps best to call them "extremity potentials" Goldberger's "augmented unipolar" limb leads have two advantages over the original Wilson leads (a) the lead connections necessitate only one electrode on each limb, and (b) the potential changes are conveniently large They omit the Wilson resistances, however, and Bryant and Johnston have

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shown that this omission introduces significant error in a small percentage of cases So, although Wilson adopted the Goldberger technique, he preferred to retain the resistances and this appears to be the most acceptable method for general use

In recording either the præcordial or the extremity potentials, it is not correct to say that the resistances are unnecessary if the skin resistance is low, the purpose of the resistances is to prevent an appreciable flow of current when there is a considerable potential difference between points coupled together —they are therefore *more* necessary if skin resistance is very low In practice, the resistances are naturally more advisable in recording extremity than præcordial potentials The Wilson resistances have the same effect as a high skin resistance in increasing the tendency to pick up alternating current. To reduce interference when recording the classical limb leads, it has always been the custom to earth the " spare ' limb through the instrument but, when either the central terminal or the Goldberger technique is used, all three limbs are required, so it is impossible to earth any of them Therefore, to reduce interference, all switches designed for recording " unipolar " leads should incorporate a connection to the *right* leg which is constantly earthed

The importance of using a considerable number of præcordial leads has been underestimated These leads reflect principally the potential changes of a small part of the ventricular muscle adjacent to the electrode, so records from three or less positions may fail to show a lesion confined to part of the anterior ventricular wall This is especially important in the recognition of anterior infarction, for only one of the six usual præcordial leads may reveal *diagnostic* abnormalities In addition, multiple præcordial leads give valuable information concerning the extent of the infarct Further, as the electrode is moved across the præcordium, the progressive changes in the ventricular complex form a regular pattern in normal subjects, and disturbances of this pattern from disease cannot always be recognized when the form of the complex is known only at two or three points Finally, it cannot be over-emphasized that the right præcordial potentials rarely influence the extremity potentials, so that anteroseptal infarction is usually associated with a normal limb lead electrocardiogram

After further discussion the Society then approved the publication of the Report as an expression of the present views of the majority of its members [The Report is published on page 103 of this number]

SHORT COMMUNICATIONS

A CLINICAL COMPARISON OF CR, CF, AND V LEADS IN HEALTH AND DISEASE

By AUBREY LEATHAM

(*Introduced by* WILLIAM EVANS)

On 500 patients, including 100 controls, leads CR CF, and V 1-7, standard limbs leads and unipolar limb leads have been taken Analysis of the chest leads on a purely practical basis has led to four main conclusions

Since the CF electrocardiogram so often appears abnormal in health it is best to forego it in routine practice

In ventricular preponderance, bundle branch block, posterior cardiac infarction, and in most cases of anterior infarction, a comparison of the CR and V electrocardiograms showed that there were

no significant differences between the QRS complexes and T waves

In 30 patients with anterior or antero-lateral cardiac infarction showing slight cardiographic changes, the abnormalities were seen more plainly in the V leads, although in only one were they absent from the CR leads

On the other hand, the T inversion commonly found in V1 in health and occasionally in V7 might be considered a disadvantage In practice, therefore, neither electrocardiogram has shown much superiority over the other

A COMPARISON OF STANDARD LEADS, UNIPOLAR LIMB LEADS, AND PRÆCORDIAL LEADS

By D R CAMERON

(*Introduced by* J H WRIGHT)

Standard limb leads, unipolar limb leads (Wilson and Goldberger techniques) and præcordial leads 1-6 of CR, CL, CF, and V (Goldberger) types were taken in 30 normal and 30 abnormal subjects

The site of the remote electrode may have considerable effect on the form of the præcordial cardiogram Any component—P, QRS, S-T or T—may be affected

In the normal case, differences are usually most obvious in the extreme right (1 and 2) or left (5 and 6) positions, where the amplitude of the deflections is small and therefore more liable to noticeable distortion They are also more obvious in P and T because (a) deflections are smaller, and (b) duration is longer than in QRS

In certain abnormal cases, the differences may be most obvious in the transitional zone (3 and 4)

Prediction of the differences in CR, CL, and CF is possible from a study of any one of them in conjunction with the S limb leads (of Wolfirth and Wood)

The V leads always occupy an intermediate position between the extremes of the other præcordial leads, i e distortion is reduced to a *minimum*

Consideration of the unipolar limb and præcordial leads renders possible a fairly accurate prediction of the CR, CL, and CF leads In the normal cases the variations depend mainly on the position of the heart In the abnormal cases they depend also on the nature and site of the lesion

Preliminary study (6 cases) indicated no significant differences in V (Goldberger) and V (Wilson) præcordial leads

The augmented Goldberger technique for unipolar limb leads seems in some cases to give larger amplitudes than could theoretically be expected, though the form of the complex is unaltered

Unipolar Electrocardiograms in Coronary Thrombosis

By Anne C Aitkenhead

(Introduced by J H Wright)

The present contribution deals with 150 cases mostly of coronary thrombosis studied by unipolar leads over the past three years In most early cases, serial tracings were taken every few days and cases studied at the beginning of the investigation have been recalled for check-up The cases have been classified according to localization of infarct after the method of Wilson and the relative frequency of the different sites has been noted

While many fit into the well recognized groups, a considerable number are atypical, e g a typical T III electrocardiogram in standard limb leads may be associated with a *small* R in leads over right side of præcordium and not the usual large R The coexistence of left ventricular hypertrophy is a complicating factor in leads over left side of præcordium but the height of R and the level of S–T help to differentiate

Serial tracings have shown the regression of an infarct from its edges inwards, thus an antero-septal and antero-lateral infarct shows most rapid signs of healing in V6 and later V5 and also in V1 and later V2 while V3 or V4 may be the last to return to more or less normal We have used V7 frequently and find it particularly useful in postero-lateral infarcts where it may be the only lead which overlies the infarct directly (albeit only its edge) Leads V5 and V6 are not infrequently redundant

Cardiac Pain with Recovery of the T Wave

By Terence East and S Oram

Published in full, Brit Heart J (1948), 10, 263

The Effect of Posture upon Normal and Abnormal Electrocardiograms

By A Morgan Jones, H K Hellerstein, and Harold Feil (introduced)

The effect of posture upon the standard limb leads, the extremity and præcordial potentials has been studied in 100 cases, 20 normal, 20 right, and 20 left bundle branch block, 20 with isolated right ventricular enlargement, and 20 with isolated left ventricular enlargement Electrocardiograms were recorded in the supine, sitting, right and left lateral positions except in the cases with bundle branch block, in which the sitting posture was not studied

In *normal subjects* the axis could be changed within wide limits in a considerable proportion of cases, sometimes over almost the whole normal range from +90° to 0°, but in no case did the axis fall outside normal limits in the postures studied The axis was usually farthest to the left in the sitting posture and to the right in the left lateral position

The changes were due to reversal of the form of the extremity potentials of the left arm and left leg, the præcordial potentials remained of the same general form, but the transitional zone rotated to the left when the axis in the standard limb leads shifted to the right   T wave changes were associated with the QRS changes

- In *left bundle branch block* very striking changes occurred, especially on turning into the left lateral position   In this posture abnormal right axis deviation appeared in 4 cases, and the limb lead cardiograms simulated right bundle branch block, the præcordial potentials remained substantially unchanged and in all positions were characteristic of left bundle branch block   The changes were much less striking in *right bundle branch block*, the limb leads being substantially of the same form in all positions

In *left ventricular enlargement* even more striking changes were present, again most extreme in the left lateral position   In that position abnormal right axis deviation appeared, and ST–T changes

appeared in lead III instead of in lead I, owing to reversal of the form of the extremity potentials of the left arm and left foot   The appearances in this position thus often simulated those of right ventricular enlargement, but the præcordial potentials remained characteristic of left ventricular enlargement   In cases with *right ventricular enlargement* the changes in the limb leads were very slight and did not simulate left ventricular enlargement in any position

The striking postural changes in left ventricular enlargement and in left bundle branch block were compared with the slight changes in right ventricular enlargement and right bundle branch block   If the amount of axis change is taken as an indication of the extent of the changes in pattern, there is a statistically significant difference between the extent of the changes in left ventricular enlargement and in normal subjects on the one hand, and between normal subjects and right ventricular enlargement on the other   Possible reasons for this difference were discussed

SUBACUTE BACTERIAL ENDOCARDITIS

BY K D WILKINSON

The Birmingham centre has treated 63 cases and has had 12 relapses   The *Streptococcus viridans* is the infecting organism in over 90 per cent of cases   Fifty-eight per cent of all cases have been cured and are alive, many at full work as before their infection

When the centre began we used a dosage of 0 25 mega units daily and met 4 cases with infections that could not be controlled   With a dosage of 1 mega unit daily for 28 days the results have been better   For a relapse 2 mega units daily for 6 weeks is the usual dose, but for one highly resistant *Streptococcus D* a dosage of 11 5 mega units daily for 6 weeks resulted in a cure   There have been no failures to cure the infection with the bigger doses

The initial symptoms of a relapse may be very slight   as patients are under supervision the relapses are detected early and treated efficiently and early   It is probable that the early symptoms of most cases of infective endocarditis are slight, and it seems most important to point out the early symptoms so that all cases may be investigated and brought under treatment as early as possible

A change in health is the first thing noticed   Fever, seldom high, sweating, especially at night, malaise, lassitude, and vague pains in back or limbs which is commonly diagnosed as influenza   Some anorexia and loss of weight occur, but these symp-

toms tend to be slight and vague   Even those who have had a similar illness before tend to say " I don't feel well "

The physical signs may be almost as slight and vague   Splenic enlargement and changes in the heart murmurs are among the most definite   Major embolic manifestations are unusual but intermittent albuminuria with blood cells and casts in the urine are quite the most frequent significant sign

There were 2 cases of hemiplegia, 1 of aphasia with no other definite nervous lesion, 2 of repeated pulmonary embolism, and 1 with glycosuria which disappeared as the infection was brought under control

The best results are obtained in those who come under treatment early   The mouth is far the most important source of infection   in eight of this series the extraction of teeth was related to the onset of symptoms so definitely that there can be no doubt that the operation acted as a trigger, but gingival infection is at least as important as apical abscesses   The patient with the resistant *Streptococcus D* whom I have mentioned as cured by 11 5 mega units daily for 6 weeks began to respond after an extensive excision of swollen infected gingival margins

Teeth and gingival infection can be treated while the patient is on the penicillin course, and this is

very important if relapses are to be avoided As might be expected, the blood urea gives some indication of the severity of renal damage Those patients with raised blood ureas do less well as a rule Hæmoglobin estimations are important Bramwell stated in his recent paper that the rate of hæmoglobin recovery was slow recalling a few individual cases I doubted this, but on working out the recovery curves of all our cases I find that the observation is perfectly correct The blood recovery rate contrasts most remarkably with the results of iron therapy in low colour-index anæmias or liver treatment in typical Addisonian anæmia In cases of infective endocarditis who had no hæmatinics or transfusion in the first month the average gain of hæmoglobin is 3 5 per cent, i e from 76 to 79 per cent In the second month all the records tend upwards, the average gain being 8 per cent, i e from 79 to 87 per cent, while in the third month the rise was 7 per cent, i e from 87 to 94 per cent

MITRAL STENOSIS IN LATER LIFE

BY HAROLD COOKSON

Results of observations on 36 cases with mitral stenosis ranging in age from 51 to 77 years were reported Women outnumbered men by 3 to 1, and most of the patients were seen in private practice A clear history of rheumatic fever or chorea was given by 13, and in a further 8 heart disease or a valve lesion had been diagnosed in early life In 4 cases the first known attack of rheumatic fever occurred at the age of 34 or later

All patients had lead normal active lives up to the sixth, seventh, or eighth decade, and 15 of the 21 married women had had children When first seen 32 patients had auricular fibrillation, and 2 auricular tachycardia, and the onset of an arrhythmia seems nearly always to coincide with the first appearance of symptoms Hypertension-was present in a high proportion

The criteria of diagnosis were given The X ray appearances of the heart and great vessels, which differ in some ways from what has been regarded as the characteristic picture of mitral stenosis, were described Prognosis, cause of death, and necropsy findings (3 cases) were dealt with The ætiology of the valve disease was considered to be rheumatic in all cases, and the reasons for the latency of the lesion until late in life was discussed Reasons were given for thinking that the diagnosis of mitral stenosis in later life is often missed

AN ARTIFICIAL CIRCULATION

BY R J S McDOWALL

This artificial circulation is a robust piece of apparatus which has been in use by medical students for a year By means of it, the main mechanical features of the circulation of the blood may be shown

The pump has the special feature that its output can be shown to depend both on its input and to a limited extent on the frequency of its stroke It consists essentially of a piece of flattened bicycle 1-inch inner tubing 4 inches long which is compressed by a moving plate controlled by a cam A large inlet " valve " of little resistance is provided by the closure of the inlet by a narrow plate driven by another cam on the same shaft just before the main stroke of the pump A very robust and simple exit valve is provided by a piece of inner tubing stretched over a piece of brass tubing into the outer end of which is inserted a wider flat piece of bakelite A visible flow indicator in the system is provided by a bent tube inside a small Kjeldahl flask, the flow being directed against the side of the flask to avoid frothing

The rate of the pump can be altered by changing the starting resistance of the motor driving the camshaft and the effects of tachycardia shown

The ' arterial " pressure taken on a mercury manometer can be altered up to 200 mm Hg by changing the filling of the heart, its rate within limits, and by varying the resistance of the system Increased filling of the heart is produced by raising the hinged part of the system to the horizontal or by compressing the ' blood depot " which is a piece of inner tube which can be rolled up The air pressure can be adjusted in the bottle so that the changes in " heart " output become visible

The " venous pressure " taken on a manometer (a narrow burette with a fountain-pen cap as a piston), can be shown to be affected by the amount

of circulating fluid, by the capacity of the system, which can be increased by unrolling the "blood depot," by the peripheral resistance, and by the output of the pump   If the pump is slowed or stopped, the "venous pressure" rises markedly as in cardiac disease

A reduction of the elasticity of the system to imitate hardened arteries provided by the inverted bottle is effected by pinching the tube and is shown

to increase the pulse pressure and render the flow in the flow-meter intermittent

A lever system from the rubber valve chamber may be added to record the rapid changes in the "arterial pressure   better than the mercury mano-meter

For making original forms of the pump and the exit valve I am particularly indebted to Dr A E Schuster

THE EFFECT OF DIGITALIS ON THE VENOUS PRESSURE
By PAUL WOOD AND JOHN PAULETT (*introduced*)
Published in full, Brit Heart J (1949), 11   83

HEART FAILURE AND TRICUSPID INCOMPETENCE
By W BRIGDEN AND E P SHARPEY-SCHAFER

It was shown previously that in cases of tricuspid incompetence mean right auricular pressure was higher than the mean pressure in a peripheral vein, a phenomenon that can be reproduced in a simple mechanical model   In cases with tricuspid in-competence it may be difficult to decide to what extent the high venous pressure results from in-competence or from heart failure   Manometric curves of right auricular pressure show a high systolic curve and indicate the diastolic pressure level   Continuous recording of pressure waves on rapid withdrawal of the catheter from auricle to peripheral vein show damping out of the systolic

pulsations in the peripheral vein   The presence or absence of heart failure may also be demonstrated by measuring the response of the forearm flow to changes in posture   In the normal subject the forearm vessels constrict on tipping into the upright posture, while in cases of left heart failure, with or without high right auricular pressures, constriction occurs in the supine position   Some cases of tricuspid incompetence show the same response of the forearm vessels as the normal subject to changes in posture, although systolic and mean right auricular pressures are high

ANGIOCARDIOGRAPHY IN CONGENITAL HEART DISEASE
By MAURICE CAMPBELL AND T H HILLS (*introduced*)

The apparatus consists of a special trolley over which an X-ray tube is located at a suitable height Just below the trolley top is a 15 by 16 inch fluore-scent screen and the image produced at this plane is recorded by a large roll-film camera

Exposures are made at the rate of one a second on a film whose width is such that the finished negatives are about 5 by 5 inches square   As many as fifty consecutive exposures could be obtained but in practice the number is normally limited to fifteen

The opaque medium used is a 70 per cent solution of diodrast in water, and a preliminary sensitivity test is carried out.

Success depends on the intravenous injection of

from 30 to 50 ml of the dye in a maximum of 2 seconds   It is usually necessary to expose a vein in the arm and insert a wide gauge canula   A preliminary injection of 20 ml of saline demonstrates the suitability of the vein and the speed with which the injection can be made   About five seconds after the injection the patient feels a sensation of heat which reaches its maximum rapidly and fades more slowly within two minutes

It is not practicable to carry out this investigation in small or nervous children without an anæsthetic, and this must add to the risk   The best anæsthetic is probably the combination of cyclopropane and oxygen   Oxygen should be continued till normal conscious respiration has been restored

In Fallot's tetralogy the interpretation of the films can be considered under two headings

Firstly, the volume shunt of blood from right to left is estimated by the degree of filling of the aorta which is generally seen as early as two seconds after the injection   The presence-of dye in the subclavian artery, the abdominal aorta, and the kidneys gives additional direct evidence of the proportion of dye taking this route

Secondly, the pulmonary arteries usually show some filling at about two seconds but the degree of stenosis cannot be assessed on this time basis alone If there is much flow of dye through the lungs their general density will show a steady increase to a maximum in about eight seconds   This estimation of the changing density of the lung fields would appear to be a more valuable observation than the actual time and degree of filling of the pulmonary arteries

The first film of the series will often show some venous backflow due to a temporary rise of venous pressure   Traces of dye may be seen in the inferior vena cava and the internal jugular vein   This abnormal pressure must be taken into account when estimating any volume shunt but is not likely to persist after the first two seconds

In cases that appear to be typical instances of Fallot's tetralogy evidence of a right to left shunt has been obtained regularly   In one case thought to be Fallot's tetralogy no right to left shunt was found and post-mortem there was high grade pulmonary stenosis with a small auricular septal defect without the other features of Fallot's tetralogy   A moderate right to left shunt has sometimes been suggested in cases that were not obviously cyanotic

Our early clinical impression is that the method is perhaps less sensitive in detecting pulmonary stenosis, presumably in cases where this is not so severe   This differentiation may prove of value in estimating the degree of success following a systemic-pulmonary anastomosis or in chosing cases suitable for pulmonary valvulotomy

In addition, a high proportion of angiocardiograms show points of interest that were not suspected—a double superior vena cava, a large pulmonary artery on one side with obstruction on the other side, and a widespread venous anastomosis on the right side   In one case regarded as tricuspid atresia with non-functioning right ventricle the angiocardiogram provided good supporting evidence

CIRCULATION TIMES IN CONGENITAL HEART DISEASE

By K D ALLANBY

(*Introduced by* MAURICE CAMPBELL)

To be published in full, Brit Heart J , April, 1949

APICAL DIASTOLIC MURMURS IN SEVERE ANÆMIA

By H E S PEARSON

A murmur closely simulating that of mitral stenosis can occur occasionally in cases of severe chronic anæmia in the absence of valvular disease Numerous references to this are found in late nineteenth century continental textbooks and articles on pernicious anæmia, and Cabot (1896) recorded 9 such murmurs in his series of 857 cases of this disease   Gunewardene (1933), dealing with hookworm anæmia, describes 4 cases in whom a confident diagnosis of mitral stenosis was disproved either by autopsy or by the disappearance of the murmur on treatment, and Klinefelter (1942) obtained graphic records of apical presystolic murmurs in patients with sickle-cell anæmia

Three cases presenting this physical sign are described, and the apparently arbitrary appearance and fugitive nature of the murmurs are shown by means of charts   This murmur has several features

in common with the transient diastolic murmur that can occur in cases of rheumatic fever (Carey Coombs, 1924) and in discussing its possible cause certain explanations that have been put forward for the latter are admissible here for consideration

With these inclusions, the following factors have been held responsible by various authors

1   Decreased viscosity of blood (Sahli, 1895, Garb, 1944)

2   Increased speed of blood flow (White and Wood, 1923) with rapid filling of atonic left ventricle (Bland, Jones, and White, 1935)

3   " Relative mitral stenosis " (White, 1937), or combination of these (Luisada, 1948)

4   Pressure of dilated pulmonary artery on mitral orifice (Kerr, 1936)

5   Pressure of dilated right and left ventricles on mitral orifice (Weinstein and Lev, 1942)

It is felt that the facts observed in these three cases cannot be satisfactorily explained in any of the above ways, although the first factor may play a part The suggestion is made that the apical diastolic murmur in severe anæmia is caused by incomplete opening of the mitral valve, associated, in the way to be described, with loss of passive tone in the papillary muscles

The stream of blood, entering the ventricle axially, recoils radially and upward towards the base of the heart, thus tending to press the mitral cusps together Closure is prevented chiefly by the lateral pressure of the entering stream but also by the passive tension of the papillary muscles on the chordæ tendinæ Only minor pressures are involved and failure of the papillary muscles to exert their normal light " spring-loading " action on the valve allows the cusps to lie so sharply curved towards one another that a murmur is produced in the narrowed commissure Fatty change, when present, is commonly maximal in the papillary muscles, and may lead to stretching

This paradoxical movement and its control by the papillary muscles can be demonstrated in the cadaveric heart by a simple experiment

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THE GRAPHIC REGISTRATION OF BASAL DIASTOLIC MURMURS*

BY BERTRAND G WELLS

(Introduced by GEOFFREY BOURNE)

The vibrations of the diastolic murmur of aortic regurgitation are of high frequency and very low energy value Other cardiac events, however, cause at the same location vibrations of lower frequency and many thousands times the energy If the phonocardiogram were to register deflections of amplitude directly proportional to the energy of these vibrations the tracing would have to be hundreds of metres wide in order to show the diastolic murmur as deflections of 1 mm in width If the amplitude of the low frequency waves is attenuated logarithmically with regard to their frequency, we are enabled to show the 1 mm diastolic vibrations clearly while the low frequency waves are all reduced in amplitude by this process of filtration, so that they can be confined to paper a few centimetres wide Workers in phonocardiography have almost always used unsuitable apparatus, and have not been able to register this murmur satisfactorily We have used a Sanborn phonocardiogram with stethoscopic and logarithmic registration, and interchangeable chest pieces, and have, with due attention to technique, been able to register every murmur audible clinically

An analysis of 50 consecutive cases with audible murmurs of aortic or pulmonary regurgitation showed much variation in pattern The frequency of the vibrations varies from moderately low to moderately high The murmur usually persists throughout most of diastole The configuration is that there is usually an early crescendo phase before the longer decrescendo phase This phenomenon is sometimes audible, but much more frequently registered, and failure to hear the early crescendo phase may be explained by study of the characteristics of the human hearing mechanism Examples of all types of basal diastolic murmur are shown, excluding the continuous murmurs of patent ductus, A-V aneurysm, and venous hum Occasional tracings are found where diastolic vibrations are registered when no murmur is audible The significance of these vibrations is obscure, but their

evaluation is helped by a comparison of their pattern with that of the audible diastolic murmur

Finally, since there is often difference of opinion among cardiologists as to whether a diastolic murmur is present or not, we consider that phono-

cardiography with proper technique may be of value in settling questions of this kind

SIMPLE CALIBRATED PHONOCARDIOGRAPHY

By G J AITKEN (introduced)

Knowledge of the frequency response of a phonocardiograph is necessary before records can be adequately interpreted Even then, comparison with records of other instruments is difficult Lack of this knowledge resulted in disagreement among earlier investigators With instruments introducing attenuation of low frequency vibrations, heart sounds appear shorter, and the third sound and possibly important low frequency components of murmurs are recorded less frequently than with instruments that register low frequency vibrations well The higher frequency murmurs, however, are more easily recorded and their moment of onset defined with just such attenuation of confusing high intensity low frequency cardiac vibrations

A simple calibrated phonocardiograph is described Basically it is a stethoscopic phonocardiograph with electrical filters enabling records to be obtained of vibrations in a " low frequency band " of 20 to 200 cycles a second, and in a " high frequency band " of 140 cycles a second upwards

It offers a fairly satisfactory solution to many difficulties in interpretation of single recordings The precise frequency characteristics of the basic phonocardiograph are less important Whatever the likely degree of attenuation of the low frequency components of the cardiac vibrations in the unfiltered phonocardiogram, they are easily recorded at suitable amplitude in the low frequency band, in the absence of all high frequency vibrations

In the band embracing frequencies greater than 140 cycles a second the predominantly higher frequency of most systolic and diastolic murmurs allow them to be recorded uninfluenced by the high intensity low frequency heart sounds The first heart sound is represented by sharply defined overtones of its second and third components, more suitable points from which to time auricular or ventricular systolic murmurs than any so far described

Examples illustrating the value of simple calibrated phonocardiography are given

A CASE OF POLYARTERITIS NODOSA SHOWING MULTIPLE CORONARY ANEURYSMS

By JOHN R H TOWERS

The case described is one of polyarteritis nodosa For years the presence of palpable nodules was regarded as an essential diagnostic criterion in this condition, but recently it has been recognized that palpable lesions of this type are the exception rather than the rule In this case the diagnosis was not so difficult but the clinical and autopsy findings were so striking as to be of interest

The patient, a motor mechanic of 39, had no important illness until 1943, when serving in the 6th Airborne Division, he developed a duodenal ulcer, which gave rise to intercurrent dyspepsia and finally to his discharge in 1945 He had intermittent dyspepsia over the last two years, but remained at his work until May, 1948, when he suddenly developed pains in both legs and difficulty in walking, and he had to go to bed Symptoms were first noticed whilst getting into a motor car These pains

were present from the knees to the feet A few days later the pain became generalized, his hands and feet and testicles became slightly swollen and painful There was in addition, swelling of the left breast which was very tender

A fortnight after the onset he was free from pain and feeling better A week later, however, he noticed his stools were black and he developed epigastric pain with some vomiting This pain was worse before meals and relieved by food, but liable to occur at any time of the day or night and to last for several hours, at times it was very severe

At this stage, i e three weeks after the onset, he had an attack of diplopia lasting half an hour, there was no previous attack and none since After this there was a return of generalized aches and pains in the limbs and back, his appetite diminished and he lost much weight His skin, normally rather

deeply pigmented, became darker in colour and he developed a sallow complexion His sleep was disturbed by pain Bowels a little constipated, micturition normal These symptoms continued unaltered until his admission to the Leeds Infirmary in July, approximately ten weeks from the onset

Examination on admission He was cachetic with pigmentation of the skin, rather suggestive of Addison's disease He had obviously lost much weight He was pyrexial up to 101° for four days and thereafter there was no rise of temperature His pulse rate averaged 100 until a day or two before his death He had what were taken to be shotty glands in the neck, axillæ, and groins, and the spleen was just palpable The blood pressure was 130/100 The urine contained a trace of albumen, but no red cells The heart was not enlarged

The blood count showed an anæmia without eosinophilia—Hb 71 per cent, red blood cells, 3,700,000, white cells, 9,600, basophils 5 per cent, polymorphs, 74 per cent, eosinophils, 2 per cent, lymphocytes, 20 per cent

The X-ray of stomach and duodenum showed an appearance consistent with duodenal ulceration The stools were negative for occult blood The Wassermann reaction was negative

Extensive investigation was carried out with no helpful finding, but shortly we discovered that the so-called glands extended down the arms, along the line of the vessels and also to a lesser extent, down the inner aspect of the thighs, and a hard, shotty mass, the size of a pea was felt through the anterior rectal wall *Biopsy* of one of the masses from the arm showed it to be a thrombosed aneurysm arising from a small muscular vessel, the wall of which showed extensive mucoid degeneration The diagnosis of periarteritis nodosa was then made The patient went gradually downhill, became emaciated, and died in September, 1948

Autopsy This was performed by Dr Carmichael and showed a striking picture A very large number of aneurysms ranging in size from 1 cm to 2 cm were seen in association with most of the principal arteries in the body, with the exception of those in the lungs and brain The lesions have all relatively thick fibrous walls and are filled with dense thrombus, mostly of dark red colour but there are also masses of pale greyish-white clot or laminated grey and red clot clinging to the walls of many of the sacs Few of the aneurysms are attached to vessels large enough to be opened up with scissors, i e they apparently spring rather from relatively small unnamed branches than from the larger trunks

Impressive examples were as follows a number of aneurysms adhering to the outer surface of the thoracic aorta and related to the intercostal arteries, a small vessel on the surface of the diaphragm at the attachment to the pericardium, where six close-set aneurysms, each 3 mm in diameter were concentrated in 3 cm of the vessel's length, a 'beading' of the anterior aspect of the bony spine by aneurysms, and numerous aneurysms along the length of the spermatic arteries

There are many large aneurysms on the right and left gastric arteries to the gastroepiploic artery The mesentary also shows dozens of aneurysms of a size varying from 2 to 3 mm to nodules almost 1 cm in diameter The aneurysms related to the stomach measure 1 5 cm and more The pelvic mesocolon shows only a very few small aneurysms and the position is similar with most of the arteries supplying various parts of the colon Right, relatively large branch of hepatic artery bears a large aneurysm, 1 cm in diameter, which is on the main stem, but there are several other similar sized aneurysms in this neighbourhood There are several aneurysms of 2 cm diameter and smaller within the head and body of the pancreas and at least two of these have ruptured, but the effused blood does not extend far into the adjacent tissue There are few aneurysms in the vicinity of the abdominal aorta The aneurysms are present on the branches of the splenic aorta in the hilum and substance of the spleen, and of branches of the renal aorta within the venal substance, also in considerable number of small size in the very large portal tracts No aneurysms on main splenic and renal arteries

The spleen contains an aneurysm fully 1 cm in diameter and one or two smaller nodules and an infarct at one pole The kidneys contain numerous thick-walled aneurysms approximately 3 to 6 mm in diameter and located chiefly in the region of the boundary zone or farther in towards the hilus There is also much recent infarction, and much irregular coarse pitting on the outer surface, probably due to scarring from an old infarction The renal tissue otherwise is mottled, mostly showing a dusky congestion, other parts are pale Large tracts of tissue are partially fibrosed

The stomach was normal apart from well-marked engorgement at the crest of the mucosal folds in places and some hypertrophy of the pylorus and large area of scarring centred over the pylorus and lesser curvature, and spreading into the stomach and duodenum

The brain and lungs, however, were normal, showing no gross change in their substance or vessels

There are numerous aneurysms connected with the coronary branches, particularly the arteries supplying the line of the interventricular sulcus, and the anterior and lateral surface of the right ventricle

At least 30 to 40 aneurysms of varying sizes are present, varying from a few mm to 2 5 cm in diameter   There is a thin layer of fibrinous exudate scattered over the whole epicardial surface   The chambers of the heart are all slightly dilated, but the myocardium has a healthy appearance and texture and shows no evidence of infarction

ELECTROCARDIOGRAPHIC STUDIES IN CRETINISM

By BERNARD SCHLESINGER AND BERNHARD LANDTMAN (*introduced*)

To be published in full, Brit Heart J , July or October 1949

A CASE OF PHEOCHROMOCYTOMA WITH SUSTAINED HYPERTENSION

By LESLIE COLE

This case is described to emphasize the fact that tumours of the adrenal medulla may cause sustained hypertension in the early stages, without giving rise to paroxysmal symptoms, or paroxysmal hypertension, to show the clinical picture in the early stages, and to comment on the use of certain diagnostic aids

The patient was a farmer's wife aged 35, with three children, and she developed sudden headache three weeks after a severe antepartum hæmorrhage This persisted daily almost without remission until her death thirteen months later   It was marked in the early morning, grew worse month by month and latterly was associated with early morning nausea, vomiting, profuse sweating, cold hands and feet, shakiness, nervousness of an unusual sort and "peculiar sensations", and during the last three weeks, muscular weakness and exhaustion   The blood pressure was first found to be raised seven months after the onset (180/130) and remained steadily at this level until just before death   Repeated clinical examination was otherwise negative and thorough investigation failed to show any cause A single paroxysm of hypertension seven days before death (260/150) revealed the probable diagnosis, but came too late to save her life   It was followed by a severe attack of right-sided abdominal pain and paralytic ileus which necessitated laparotomy and cæcostomy   At operation, a tumour was found at the site of the left suprarenal gland which subsequently proved to be a typical pheochromocytoma This was removed a week later but the patient succumbed   Autopsy showed that the right-sided pain was due to a large infarct of the right kidney

Diagnosis is difficult and involves recognition of the syndrome produced by hypersecretion of adrenalin and localization of the tumour or tumours For the first, it is essential to realize that sustained hypertension is indistinguishable from the essential or malignant type and without paroxysms may be present in the early stages, and also to appreciate the significance of the symptoms illustrated by this case   In this and many others recorded there are unique clinical grounds for suspecting the diagnosis once the clinician is aware of the syndrome   Goldenberg's benzodioxane test then appears to be of great value in confirming it, but this patient died before his paper had been published   To localize the tumour, an intravenous or retrograde pyelogram may be sufficient, but perirenal insufflation may be necessary, or even exploration   Here, although the symptoms and signs pointed to a right-sided lesion, the tumour was on the left   Early diagnosis and accurate localization are extremely important because successful removal may be expected to give complete cure

THE Q–T INTERVAL IN ACUTE RHEUMATIC CARDITIS

By D G ABRAHAMS

(*Introduced by* PAUL WOOD)

To be published in full, Brit Heart J , July or October 1949

MULTIPLE UNIPOLAR LEADS

REPORT OF THE COMMITTEE OF THE BRITISH CARDIAC SOCIETY

The British Cardiac Society at its recent meeting approved the publication of the following report as an expression of present views of the majority of its members

The Council had asked the committee, consisting of Terence East, I G W Hill, Curtis Bain, and Paul Wood to draw up such a report that might help those who wished to have information about present practice Obviously, they have no wish to limit in any way investigations into new and important methods but feel that where routine work, rather than research, is concerned, there are advantages in some degree of uniformity in leads presented, and in the way they are mounted

It is, perhaps, too soon to reach any final recommendation in this last direction and various suggestions made at the meeting were considered (see Proceedings, p 92) The Editor would be grateful if those submitting papers would generally try to use one or other of these methods, and a figure that is 4½–5½ inches wide is generally easier to print and better looking than one that is tall and narrow

<div align="right">EDITOR</div>

REPORT OF COMMITTEE

Although multiple leads from a series of points across the præcordium are in general use in this country, there is so far only one position for the præcordial electrode defined as standard Single præcordial lead used as routine may afford scanty or even misleading information, and multiple leads are essential

Bipolar chest leads It is suggested that the use of the bipolar chest leads CR and CF be discontinued The distal electrode in the case of CR introduces a positive error, and in the case of CF an error that may be positive or negative, depending on the position of the heart

UNIPOLAR CHEST LEADS

Unipolar V leads avoid this error The switch is set for lead 1 The exploring or præcordial electrode is attached to the left arm wire of the cardiograph It is then paired with a central terminal (right arm wire of the cardiograph) connected to the right arm, left arm, and left leg. The potential of the central terminal will practically be zero, by Einthoven's formula, as shown by experiment The original method of Wilson connects each of the limbs to the central terminal through equal resistances of at least 5000 ohms The method of Goldberger omits the resistance

The Burger suction electrode (2 cm in diameter) is convenient for the exploring præcordial electrode

Positions The position of the præcordial electrode is indicated by a numeral used according to the following plan V1 shall be used for the right margin of the sternum, in the fourth intercostal space V2 for the left margin of the sternum at the same level V4 for the mid-clavicular line in the fifth intercostal space V3 for a point midway between 2 and 4 V5 for the left anterior axillary line V6 for the mid-axillary line, positions 5 and 6 are on the same level as 4 V7 is the posterior axillary line, and V8 below the apex of the scapula at the same level

VE is used for an epigastric lead below the xiphisternum

RUA stands for a position on the right costal margin just to the right of the midline

The corresponding V positions to the right are shown by the letter R, e g V3R

Standardization As the voltages of V leads are often high it may be convenient to use half standardization ($1mV = 5$ mm) in order to confine the deflections to a convenient size If this reduced sensitivity is used it should be employed uniformly in all chest leads, and indicated N/2

UNIPOLAR LIMB LEADS

The augmented unipolar limb leads of Goldberger are obtained by putting the exploring electrode, attached to the left arm wire of the cardiograph, the switch being set for lead 1, on the appropriate limb

<div align="center">103</div>

The other two limbs are connected to the central terminal, which is attached to the right arm wire of the cardiograph   The deflections are 50 per cent larger than those obtained by the Wilson method The Goldberger technique is satisfactory   The tracings are labelled a VR, a VL, a VF

In order to correlate standard limb leads and unipolar limb leads, it is helpful to recall that lead 1 is VL–VR, lead 2 is VF–VR, lead 3 is VF–VL, and that by the Goldberger technique a VL is $\frac{1}{2}(I-III)$, a VR is $-\frac{1}{2}(I+II)$ and VF is $\frac{1}{2}(II+III)$

SELECTION OF LEADS

The full electrical exploration of the heart involves the taking of at least twelve leads, and sometimes more   The twelve basic leads are (1) the three standard limb leads, (2) the three unipolar limb leads, and (3) the six unipolar præcordial V leads

Until familiarity with the appearances of the deflections in the various leads in different conditions is obtained, these twelve should be recorded as a routine

In practice the taking of twelve leads is laborious and time-consuming, and involves the use of many films   It is possible to limit the leads recorded to a selected few when a particular lesion is suspected Films may be economized also by exposing half a strip at a time when the Cambridge instrument is used, and so obtaining six tracings on one film

The following suggestions may help in selecting leads likely to be most useful in the diagnosis of various lesions   For the preliminary routine approach it may be enough to select V1 or V2 and V4 and V5 or V5 and V6 depending on the size of the heart, and VL and VF   These may suggest what further records are needed for full electrical exploration   The clinical findings may suggest special leads

It is important to record potentials from the surface of the left ventricle, this may necessitate the use of leads V6 or V7 when the interventricular septum is displaced to the left, or when there is clockwise rotation of the heart about its longitudinal axis (viewed from below)

Unipolar limb leads are particularly useful in showing the position of the heart, the combination of VL and VF is best for this

VF shows auricular activity well, and so is useful for auricular arrhythmias, it is also useful for posterior infarcts

VL shows lateral infarcts

VR is of less value and may generally be omitted

Right ventricular leads   V1 and V2

These show best
1   Some infarcts of the myocardium
2   Right bundle branch block
3   Right ventricular hypertrophy
4   Massive pulmonary embolism
5   Auricular arrhythmias (V1 particularly)

Left ventricular leads   V4–6

These show best
1   Some infarcts of the myocardium
2   Left ventricular hypertrophy
3   Left bundle branch block

Myocardial ischæmia   V1 V2 V3 V4 V5 V6 VL VF

Infarction can usually be detected and defined by V2–V6 and VL and VF   For high antero-lateral infarction records may be taken in the third and fourth interspaces vertically above V4, V5, and V6 VF is useful for distinguishing posterior infarction from other Q III patterns, particularly those due to transverse position of the heart, or to massive pulmonary embolism

Bundle Branch Block   Right   V1 V2

Left   V5 V6 V7, according to the degree of enlargement to the left

Massive Pulmonary Embolism   V1 V3 V5 VF

Pericarditis   V1 V3 V5

Auricular Arrhythmias   V1 and VF

Mounting of records   The V præcordial leads are most conveniently shown, horizontally in numerical order, with V1 as the first record

TERENCE EAST   I G W HILL
CURTIS BAIN   PAUL WOOD

Maternal Congenital Heart Disease as an Obstetric Problem C. J Lund *Amer J Obstet Gynec*, 55, 244–261, Feb , 1948

Details are given of a study of 25 cases of pregnancy complicated by congenital heart disease, 29 infants in all being delivered There were 13 with a patent ductus arteriosus, 8 with interventricular defect, 4 with inter-auricular communications 1 with pulmonary stenosis, and 4 of undetermined type Toxæmia was a common and severe complication Premature delivery took place in over 25% Labour tended to be shorter than the average, and forceps delivery was resorted to in over one-third of the cases although half of the patients were multiparæ All patients were classified according to the functional groups of the New York Heart Association, before pregnancy, during the first 3 months and the last 3 months, during labour, and later in the puerperium The blood pressure, vital capacity, venous pressure, and circulation times were investigated in many of the patients It was found that decrease of vital capacity was most valuable in prognosis A sudden fall in blood pressure was noticed repeatedly soon after confinement and gave rise to considerable anxiety, the mechanism of this is discussed A patent ductus arteriosus was found to be the most serious of the congenital cardiac complications All but 1 of the cases of cardiac failure were associated with this lesion, as was also the only fatality

Braithwaite Rickford

The Occurrence of Paroxysmal Cardiac Arrhythmia Following Air Embolism C Gobin *Arch Mal Cœur*, 40, 482–484, Nov –Dec , 1947

A student was entrusted with the operation of transfusing a donor s blood directly into the veins of a patient with septicæmia He thrust the recipient s needle into the veins of the donor though fortunately failed to enter the veins of the septicæmic patient with the other needle The subsequent attempts to carry out the transfusion caused the injection of about 200 ml of air into the veins of the donor but no blood. The donor, whose arm veins became inflated was alarmed and eventually brought the operation to an abrupt end by pulling out the needle and releasing the tourniquet His veins deflated but he was seized with a tickling sensation in the throat, with cough and violent dyspnœa He lost consciousness for 4 to 5 minutes and did not recover his health for some days For 5 months after this accident he was subject to attacks of paroxysmal tachycardia or palpitation lasting from a few seconds to a few minutes The radiograph of his chest revealed a slight left ventricular hypertrophy Eventually he had an attack of arrhythmia lasting for days and an electrocardiogram showed auricular fibrillation

He had no subsequent attacks and later acted again as a blood donor

The author considers this to be an instance of an autonomic excitation initiated by the presence of air in the pulmonary vessels *H E Holling*

Effect of Intravenous Cytochrome C on Capacity for Effort Without Pain in Angina of Effort H Barst and S H Rinzler *Proc Soc exp Biol , N Y ,* 67 531–533, April, 1948

Cytochrome C enhances the uptake of oxygen by the tissues When injected intravenously it is capable of restoring to normal an electrocardiogram in which changes have been produced by inhalation of a 10% oxygen mixture The authors have shown that cytochrome C in 50-mg. doses given intravenously to patients suffering from angina of effort is unable to increase their capacity for effort without pain *A I Suchett-Kaye*

Treatment of Hypertensive Vascular Disease with Rice Diet W Kempner *Amer J Med ,* 4, 545–577 , April, 1948

For the past 4 years the author has advocated a rice-fruit–sugar diet in hypertensive vascular disease and all forms of nephritis This diet contains in 2000 calories, not more than 5 g. of fat, 20 g of protein, 200 mg. of chloride, and 150 mg of sodium. All fruits and fruit juices are allowed, sugar and dextrose are unrestricted, and supplementary vitamins are given The effects of this diet on the blood and urine chemistry, blood pressure, heart size and electrocardiogram, œdema, and retinal arteriopathies in several hundred patients are recorded and illustrated by typical examples [It is extremely doubtful if the inferences which the author draws from his data would stand up to strict statistical scrutiny]

Henry Cohen

Coexisting Auricular Fibrillation and Complete Heart Block. E A Haunz and H L Smith *Amer J Med ,* 4, 237–242, Feb , 1948

A series of 10 cases of auricular fibrillation and complete heart block, all in patients with advanced cardiovascular disease, were studied The authors two main points are that (1) the presence of this combination, in the absence of a digitalis effect, implies a serious prognosis, (2) it is important to distinguish heart block due to intrinsic cardiac disease from that due to digitalis In cases in which symptoms of digitalis intoxication are slight or absent the distinction can be made by observing serial electrocardiograms *R. T Grant*

Correlation Between the Effect of Quinidine Sulfate on the Heart and Its Concentration in the Blood Plasma R WÉGRIA and M N BOYLE. *Amer J Med*, 4, 373–382, March 1948

It was found that after administration of a single oral dose of quinidine to patients with auricular fibrillation the effect on the circus rate of the auricle was roughly parallel to the quinidine concentration in plasma but no strict quantitative relation existed For example 2 hours after oral administration of 0 8 g. of quinidine sulphate the circus rate fell from 402 to 285 a minute and the plasma concentration of quinidine was 2 6 mg per litre, whereas 10 hours after the administration of quinidine the circus rate was practically the same, 292 a minute, but the plasma concentration was only 1 3 mg per litre From a further series of experiments on dogs it is concluded that such quantitative discrepancies are due to the fact that the effect on the heart is not proportional to the concentration of drug in either the plasma or the myocardium Indeed, an excessive increase in the concentration in heart tissue leads to a decrease in cardiac effect   *T Semple*

Electrocardiographic Patterns of Ventricular Aneurysm E GOLDBERGER and S P SCHWARTZ *Amer J Med*, 4, 243–247, Feb , 1948

In a series of 40 cases of myocardial infarction with and without ventricular aneurysm, all the cases with aneurysm were associated with an upward QRS complex in the right arm lead of the electrocardiogram This suggests that absence of this feature in a case of myocardial infarction indicates absence of aneurysm *R T Grant*

The Arterioles of the Skin in Essential Hypertension. E M FARBER, E A HINES, H A MONTGOMERY, and W McK CRAIG *J invest Derm*, 9, 285–298, Dec., 1947

The authors review earlier studies on the arterioles of patients with hypertension, and present a comparable study of the arterioles of the skin The wall to lumen ratio is lower in the hypertensive group, with a mean of 1 57 (70 cases), against 2 14 in the 52 control cases, there is, however, considerable overlapping Moritz and Oldt (*Amer J Path*, 1937, 13, 679) have already shown that the thickening of the wall and narrowing of the lumen which commonly indicate a state of hypertension may be completely absent in cases with hypertension of long-standing Conversely they find (in agreement again with Moritz and Oldt) that arteriolosclerosis may exist in the absence of hypertension and without any obvious correlation with age   *A C Lendrum*

Secondary Malignant Disease of the Heart. R. W RAVEN *Brit J Cancer*, 2, 1–7, March, 1948

This paper analyses 51 cases of secondary tumours in the heart or pericardium from the necropsy records of the Royal Cancer Hospital The primary tumours were distributed amongst most of the organs of the body Carcinoma of the breast was the commonest primary tumour (14 cases), secondary growth usually involved the pericardium, alone or together with the heart muscle, and was sometimes first manifested many years after radical extirpation of the primary tumour, periods of 5 and 16 years being recorded

The pericardium was sometimes normal save for an isolated secondary tumour, but otherwise pericardial effusion fibrous obliteration, or obliteration by massive deposits of tumour were found Hydrothorax and ascites resulted from cardiac failure The symptoms sometimes resembled those of subacute bacterial endocarditis Dyspnœa, tachycardia, and cardiac irregularities such as auricular fibrillation or flutter were frequent outstanding signs Some symptoms were attributable to the location of the tumour, causing heart-block, or to pericardial or pleural effusion but were not pathognomonic and further investigations were required to establish the diagnosis, including paracentesis for pericardial effusion and cytological examination of the fluid for tumour cells, radiological examination of the heart including tomography, and electrocardiography, the value of this last proceeding is emphasized When the primary tumour is known to be radiosensitive, high voltage x-irradiation may be useful in the diagnosis and treatment of cardiac secondary growths   *L Foulds*

" Functional " Subclavian Arterial Murmur Possible Relation to Scalenus Anticus Syndrome, Costoclavicular Compression, or the Neurovascular Syndrome of Wright. R B POMERANTZ *Ann Surg*, 127, 688–695, April, 1948

In a routine examination of 2619 candidates in Texas the author discovered 20 females and 1 male in whom there was a systolic murmur over the subclavian artery (or arteries) The first 11 cases were dismissed as cases of functional murmurs, but the other 10 received more detailed examination The murmur predominated on the left, appearing on that side alone 11 times, it appeared on the right side alone once, bilaterally 5 times, and in 4 cases the side was not noted General medical examination and radiographs of the chest were negative, except in 1 case where there was inactive apical tuberculosis on the opposite side to the murmur The murmur is constant, fairly loud and definite, and accentuated by deep inspiration or gradual abduction of the arm The greater the abduction the louder the murmur up to 135 to 150 degrees, when it disappeared because the blood flow to the arm had ceased No case was observed which was thought to be a scalenus syndrome, and in only 1 was the murmur thought to derive from costo-clavicular compression The presence of the murmur when the subject is in a relaxed sitting position suggests some as yet undefined mechanism by which the artery is obstructed even before abduction begins The preponderance on the left side would indicate an anatomical variation, but in the absence of symptoms surgical exploration was not thought to be justified and the question of causation is unsettled   *H T Simmons*

Elementary Atlas of Cardiography H WALLACE-JONES, E NOBLE CHAMBERLAIN, and E L RUBIN John Wright and Sons, Ltd , Bristol, 12/6

This little book does not pretend to be anything more than its title implies A short descriptive text introduces each series of cardiograms, which are beautifully reproduced and clearly annotated However, no attempt is made to outline the elementary physics of electrocardiography, and a description of unipolar leads is entirely omitted A brief essay on cardiac radiology precedes a well selected and representative collection of excellent radiograms, which includes all the more common cardiac conditions The reproduction of these plates is of the highest quality, and indeed the whole volume reflects great praise on the publishers The omission of an index is regretted *J L Loulbond*

Seasonal Variations in Heart and Coronary Disease as Related to Various Environmental Factors H R BROWN and R PEARSON *Amer Heart J* , 35, 763–768, May, 1948

A study of the vital statistics for the city of New York from 1934 to 1944 reveals that the death rate from heart disease, particularly coronary disease, is inversely related to the rise of monthly temperature, and not related to the relative humidity of the atmosphere *H E Holling*

Experiences with a New Synthetic Analgesic, Amidone Its Action on Ischemic Pains of Occlusive Arterial Diseases R J POPKIN *Amer Heart J* , 35, 793–799, May, 1948

' Amidone " (methadon, " physeptone ") (6-dimethyl amino-4, 4-diphenyl 3 heptanone hydrochloride), which resembles morphine in its action, was given to a number of patients with peripheral vascular disease who suffered from pain at rest. The dose was 5 to 15 mg by mouth The drug relieved the pain at rest but was ineffective in intermittent claudication One of the 18 patients developed a hæmorrhagic urticaria and ambulant patients suffered from light-headedness, nausea, and vomiting *H E Holling*

Effect of Sympathectomy on Blood Flow in the Human Limb I D STEIN, K. HARPUDER, and J BYER *Amer J Physiol* , 152, 499–504, March, 1948

A comparison was made by the use of plethysmographic methods of recording, of the blood flow in the foot (predominantly skin) and calf (predominantly muscle) in human patients, before and after sympathectomy of the lower limbs for peripheral vascular disease The results show that, whereas the blood flow through skin was increased by sympathectomy, that through muscle was relatively unchanged Exercise, local heating, and arterial occlusion and release were effective stimuli in increasing blood flow through sympathectomized muscles, suggesting that vasodilators of metabolic origin, and not the innervation, are important factors in the blood supply of muscles The results indicate that sympathectomy is of value clinically for increasing the blood flow through skin, but not through muscle

R A Gregory

Measurement of the Total Transverse Diameter of the Heart by Direct Percussion W D STROUD, M W STROUD, and D S MARSHALL. *Amer Heart J* 35 780–786, May, 1948

In 333 examinations of 305 patients the transverse diameter of the heart as measured by direct percussion was compared with that obtained from a teleradiograph 74% of the values obtained from percussion were within ±10% of the values obtained from radiography and 88% were within ±15% of the radiographic values Fifty-five comparable examinations on 45 women gave similar results The clinical method of percussing the heart size appears therefore to be of value *H E Holling*

Perforation of the Infarcted Interventricular Septum Report of Two Cases, one Diagnosed Antemortem N O FOWLER and R B FAILEY *Amer J med Sci* , 215, 534–541, May, 1948

Two cases of perforation of the infarcted interventricular septum are reported In one of them the diagnosis was made during life A review of reported cases revealed 56 similar, in 15 of which the diagnosis was made during life The condition should be suspected in any patient who shortly after a myocardial infarction, suddenly develops a systolic thrill and murmur in the third and fourth intercostal spaces just to the left of the sternum These patients tend to develop right ventricular failure In 38 cases the survival time was described, this being less than a month in 31 A further 6 patients died within a year, and 1 patient lived 4 years and 10 months Out of 45 patients examined 43 had a systolic murmur, which in 22 was associated with a thrill Rupture of a papillary muscle following infarction may be confused with this condition, but in the former the murmur tends to be heard best nearer to the apex, the patient s condition deteriorates rapidly, and the heart failure is left-sided rather than right-sided

C Bruce Perry

Blood Volume and Sympathectomy in Hypertension W D DAVIS and H S MAYERSON. *Proc Soc exp Biol* , N Y , 68, 117–120, May, 1948

Blood volume changes were investigated in 20 patients with hypertension who had undergone sympathectomy There were 11 women and 9 men, their ages ranged from 22 to 50 years and the periods of follow up from 3 to 18 months Plasma volume was measured photocolorimetrically with the T 1824 dye, whole blood and red cell volumes were calculated from hematocrit readings (Wintrobe) No consistent post-operative changes in the blood volume were found, and no consistent deviation from " normal " values was observed pre-operatively It was noted that in 5 patients in whom the red-cell volume was low before operation the response to sympathectomy was poor, whereas in 5 patients in whom the red cell volume was normal, or above normal, the results were good. In patients with long-standing vascular disease there was a tendency to low blood volume

A Schott

The Use of Vitamin E in Heart Disease S BAER, W I HEINE, and D B GELFOND *Amer J med Sci*, 215, 542–547, May, 1948

The effect of vitamin E orally in doses of 300 to 400 mg daily was observed in 22 patients with various forms of heart disease The authors conclude that, although their numbers are few, they cannot, from the evidence, recommend vitamin E in the treatment of congestive heart failure, angina pectoris, or hypertension

C Bruce Perry

Adreno sympathogenic Heart Disease (Neurohormonal Factors in Pathogenesis and Treatment) W RAAB *Ann intern Med*, 28, 1010–1039, May, 1948

The author points out that mechanical overload is not necessarily the whole explanation of hypertensive heart disease Many of the features of hypertensive heart disease may be found without hypertension He calls attention to the possible pathogenic role of adrenaline and allied substances Adrenaline intensifies the oxygen consumption of the heart, and may induce a state of anoxia, identical with experimental anoxia in diseased human hearts and in animal hearts after severe exercise The author considers that anginal attacks are accompanied by abnormal elevation of the adrenaline sympathin levels in the blood Hypertensive heart disease is not necessarily accompanied by any rise in adrenaline level in the blood, but abnormally high elevations of the levels of this and similar substances may follow physical exercise in patients with hypertension The electrocardiographic features of hypertensive heart disease are similar to those which result from the injection of adrenaline, and it is emphasized that the abnormal electrocardiogram may revert to normal after sympathectomy, even if the patient remains hypertensive The author develops similar arguments to account for changes in the heart in uræmia, thyrotoxicosis, and beriberi These arguments are supported by a very extensive bibliography of 235 references   *J McMichael*

Endocardiac Potentials in Right Heart Hypertrophy Comparison with the Oesophageal Electrocardiogram P SCHLESINGER, A BURLAMAQUI ENCHIMOL, and M R COTRIM *Arch Clin* 6, 139–155, March, 1948

Battro and Bidoggia have drawn attention to the similarity of the ventricular complex with the electrode in the right auricle and with the oesophageal lead in both healthy and diseased subjects This paper deals with 5 cases of right-sided hypertrophy The electrode, attached to a fine insulated wire, is introduced through the right external jugular vein, " sodium amytal being used as premedication There were no untoward effects, penicillin being given subsequently for 48 hours Standard, unipolar, and præcordial leads, and leads with the electrode at different intra-auricular and intra ventricular levels were taken The P wave is negative with the electrode at a high auricular level and gradually becomes positive as the electrode passes into the ventricle, the QRS complex at auricular level was positive in 3 cases

and negative in 2 The ST segment was elevated in 3 cases when the electrode was in the ventricle The oesophageal leads, taken at auricular level, were found to have QRS complexes similar to those taken at intra-auricular level Very similar complexes were also found with the unipolar VR lead Some anomalous changes were thought to be due to the impulse passing over the wall of the interventricular septum   *Paul B Woolley*

Influence of Hypotension on Coronary Blood Flow, Cardiac Work and Cardiac Efficiency J E ECKENHOFF, J A HAFKENSCHIEL, E L FOLTZ, and R L DRIVER *Amer J Physiol*, 152, 545–553, March 1948

In lightly anæsthetized intact dogs, coronary blood flow was measured by the nitrous oxide method, coronary sinus blood being obtained by catheterization Cardiac output was estimated by the direct Fick method Hypotension was produced either by the subarachnoidal injection of procaine solution or the intravenous injection of tetræthylammonium chloride A decrease in cardiac output and cardiac work (cardiac output × aortic pressure) occurred Coronary blood flow decreased but the rate remained relatively high in relation to the decreased work Cardiac efficiency (work/oxygen consumption) was reduced but there was no evidence that the heart was less able to perform the work required of it that is, that the hypotension was harmful to the heart

R A Gregory

The Course of Beriberi Heart Disease in American Prisoners-of war in Japan. R J ALLEMAN and G H STOLLERMAN *Ann intern Med*, 28, 949–962 May, 1948

It is generally thought that heart disease due to beriberi is accompanied by right heart enlargement and manifestations of a rapid circulation, and that a response to aneurin (thiamin) therapy is diagnostic More recently, the diagnosis has been made when there is evidence of gross dietetic deficiency together with peripheral neuritus in the presence of an enlarged failing heart for which there is no other explanation Even failure to improve with aneurin does not exclude the diagnosis Should the heart respond well to the specific vitamin relapses may still occur

Two cases are described In the first, there was a gross nutritional inadequacy, with widespread œdema, cramps in the legs, and incoordination The patient improved on treatment with the ordinary cardiac remedies, with aneurin, but very quickly relapsed A further improvement occurred for a time, but in a third attack he died Apart from some degeneration of the myocardial fibres and infiltration with small round cells no other explanation of the failure was found at necropsy In the second case the onset was similar, but the patient made a good recovery when given an adequate diet and large doses of vitamins orally and parenterally The symptoms cleared up at the end of 4 months

J McMichael

ARTERIOVENOUS ANEURYSM OF THE LUNG

BY

CHARLES BAKER AND J R TROUNCE

From Guy s Hospital

Received October 21 1948

Arteriovenous aneurysms in the lesser circulation produce a clear-cut clinical picture and illustrate again that we do not know how commonly conditions occur until they are first described The number reported since Rodes paper in 1938 indicate that it is by no means rare and it is a condition that can be successfully treated It is striking, however, that although a congenital lesion, often with obvious evidence from early years, it has so far been diagnosed almost exclusively in adults The recent interest in cyanotic congenital heart disease, which has followed the possibility of operative treatment, may well reveal further cases as it did in the examples here described It is to stress the importance of earlier recognition of a treatable condition that we are reporting two cases and reviewing the present knowledge of this disease

THE FIRST CASE

D C , aged 27, was referred to Guy s in September 1947 as a case of cyanotic congenital heart disease to see if he was suitable for a Blalock-Taussig operation He was the youngest of five children and there was no history of a similar condition in his family Cyanosis, which was gradually and steadily progressive, was noticed at the age of 4, and a year later a diagnosis of congenital heart disease was made His school life was restricted more by medical advice than by ill-health or disability At 14 he left school and worked first as an errand boy using a bicycle, but after a year he was forced to take less active employment His working life finished at the age of 19 when he was a shop assistant—work that he could do without distress—and at this time he was still cycling five miles a day One day he tripped up in the shop and fell, and this accident was mis-diagnosed by his employer as a fit He was dismissed as a potential liability His cyanosis, which was by now extreme, prevented his finding other employment, much as he

desired and sought it, and he remained at home until September 1947, when hope of relief for his supposed congenital heart condition brought him to hospital In this eight years there was gradual deterioration of his condition A year before he was seen he had tried to cycle again and found he could barely manage a mile, and by the time he was admitted he could only walk 100 to 400 yards on the level Œdema of the ankles had been almost continuous for the last four years and there was cough without sputum In 1943 he was admitted to hospital with nose bleeding and this had continued at intervals particularly in hot weather For the last two years he had attacks about once a month, particularly after bending down, when he felt weak ' with a film over the left eye and sizzling in the ears ", there was no giddiness or loss of consciousness and the attack lasted ten minutes Careful questioning could not elicit any story of hæmoptysis He did not squat on his haunches when breathless or distressed

On examination he was a spare well-built man, 5 ft 7 in in height and 112 lb in weight He was grossly cyanosed with a blotchy, pitted face as seen in seborrhæic subjects, there was very marked clubbing of fingers and toes (Fig 1 and 2) He was breathless on slight exertion but there was no orthopnœa His neck veins were not distended, the liver was just palpable but not tender, the lung bases did not sound wet, but there was slight pitting œdema of the ankles The pulse was regular The heart showed no clinical enlargement, which is not against a diagnosis of Fallot's tetralogy but with this in mind one was surprised to find an absence of any murmur, pulsation in the second left intercostal space was the only finding of note The blood pressure was 105/80 in the arms and 170/110 in the legs Screening showed a heart slightly enlarged (13/25 cm) with the pulmonary conus prominent and an enlarged right ventricle In the right lower lung field was a circumscribed shadow with a well-defined margin, calcified in its lower and

109

Fɪɢ 1 —Case 1, aged 27, showing deep cyanosis and cutaneous angiomata

lateral part   This was connected to the right hilum by a well-marked vascular shadow and there was pulsation from hilum to the tumour, which itself did not appear to pulsate, the vessels of the left hilum were not increased (Fig 3A)   The electro-cardiogram (Fig 7) showed marked right axis deviation with broad and prominent P waves in leads I and II and an inverted T in lead III

After the shadow in the lung had been seen, the two important points needed to clinch the diagnosis of arteriovenous aneurysm were looked for, and found   On listening at the right base posteriorly there was a well-marked localized systolic murmur, but no diastolic element   Angiomata were found on the inner side of the lips and on the buttocks (Fig 4) and it was clear the seborrhœic disfigurement of the face had masked further small angiomata though the smaller ones were still difficult to see owing to the intense cyanosis (Fig 1)   A diagnosis of arteriovenous aneurysm of the lung was made,

and he was admitted in February 1948 for further investigation with a view to operative treatment

The blood picture showed marked polycythæmia with 7 5 million red cells, a hæmoglobin of 140 per cent, and a hæmatocrit of 90, the white cells were 8000 per cu mm with a normal differential count   The circulation times were done by Dr Allanby, the arm to tongue time with decholin being 14 sec and arm to lung time with paraldehyde being 8 5 sec, both lying within normal limits Probably the viscosity of the blood due to his polycythæmia nullified any tendency to a quickening of the circulation rate due to the shunt   The vital capacity was 2 5 litres   Unipolar limb and chest leads showed a vertical heart but no evidence of right ventricular hypertrophy   The blood volume was calculated by Dr Reeve, the volume of red blood cells being measured by injecting a known amount of radioactive red cells   He points out that owing to the abnormal mixing of the blood the
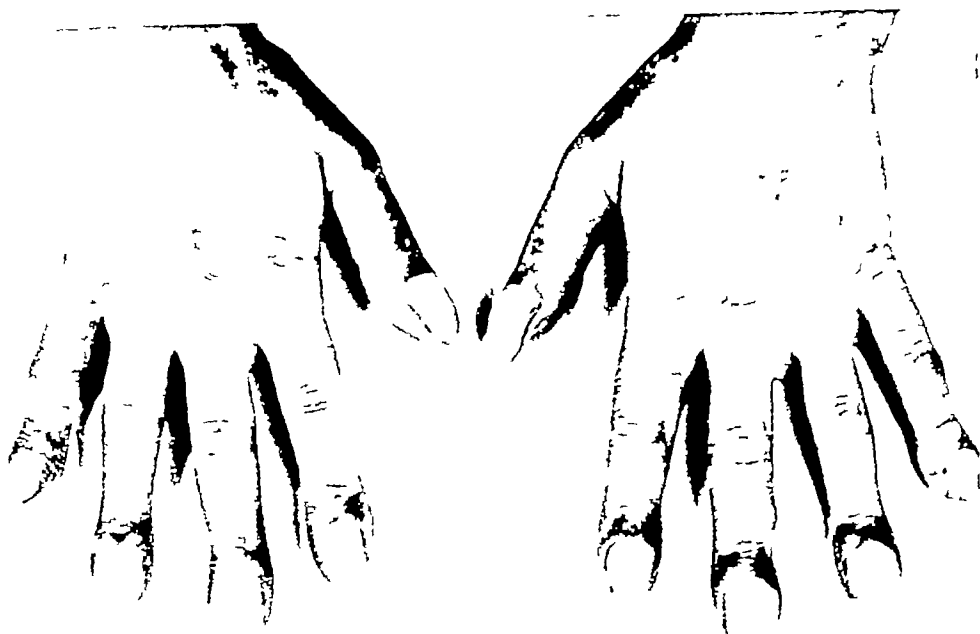
FIG 2.—Case 1, showing clubbing of the fingers

A

B
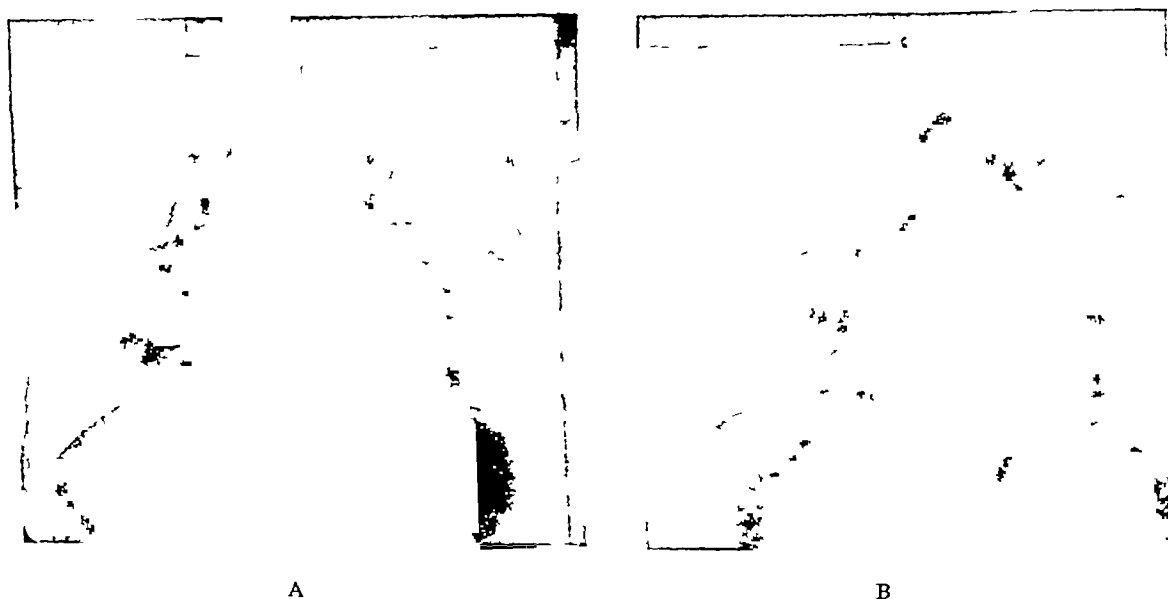
FIG 3.—Case 1 (A) Straight X-ray with partly calcified aneurysm attached to right hilum by vascular shadow (B) Angiocardiogram at 2 sec showing two additional vascular tumours, one in the right lower zone near the mediastinum and a small one in the left lower zone behind the heart shadow

FIG 4 —Case 1   Buttocks showing angiomata

figures are approximate, but a red blood cell volume of 6960 ml and a total blood volume of 8580 ml show an increase above normal

The angiocardiogram taken by Dr Hills showed well the filling of the opacity previously seen and in addition two further vascular tumours, one in the right lower zone nearer the mediastinum and a small one in the left lower zone behind the heart shadow (Fig 3B)   X-ray films of hands and feet showed no pulmonary osteopathy

Cardiac catheterization was done by Drs H E Holling and G Zak and both branches of the pulmonary artery were entered without difficulty, and the findings are summarized in Table I

The finding of a normal pressure in the right auricle is interesting in view of the suggestion of cardiac failure furnished by the slight œdema of his ankles   The lower pressure in the right pulmonary artery may be a consequence of the lower peripheral resistance offered by the hæmangioma on that side The general opinion that the peripheral resistance of lung vessels is negligible is against this view, but the blood was extremely viscous and the difference in peripheral resistance of the two lungs was probably great

Estimations of the cardiac output and of the quantities of blood passing through the pulmonary hæmangiomata were made

Cardiac Output = Oxygen Consumption *divided by* the Oxygen Content Pulmonary Vein (Arterial Blood) *minus* Oxygen Content Pulmonary Artery (ml /litre)

$$= \frac{230}{231 - 212} = 12 \text{ litres}$$

Assuming that the blood passing through the pulmonary capillaries becomes 95 per cent saturated with oxygen, the pulmonary capillary circulation was estimated as 2 6 litres

TABLE I

RESULTS OF CARDIAC CATHETERIZATION

	Inferior vena cava	Superior vena cava	Right auricle	Right ventricle	Pulmonary artery Right	Pulmonary artery Left	Brachial artery
Oxygen content (Vol per 100 ml)	23 6	21 1	21	20 6	21 2	21 3	23 1
Percentage saturation	74	66 6	66 4	65 2	67 1	67 3	73
Pressure, mm Hg	8	—	8	17	12	15	105/80

The pulmonary shunt equals the cardiac output less the pulmonary capillary circulation, i e 9 4 (12—2 6) litres a minute, which is 80 per cent of the cardiac output

This estimation of the proportion of blood passing through a shunt in the circulation is surprising but is not impossible considering the depth of the cyanosis   It compares reasonably with estimated shunts in badly cyanosed congenital hearts and with arteriovenous fistulæ of the systemic circulation The assumed figure of 95 per cent saturation of the blood after passage through the lung capillaries seems reasonable since the cyanosis of the patient did not lessen when he breathed oxygen   Even if a figure of 85 per cent saturation is assumed the shunt would still prove to be 70 per cent of the cardiac output

Mr R C Brock operated on April 5, 1948, with an anæsthetic of intratracheal cyclopropane and curare by Dr Hutton   A right posterolateral thoracotomy found the upper and middle lobes free but the lower lobe was bound down to the chest wall and diaphragm by many collateral vessels Some calcification could be felt on the surface and within the substance of the lower lobe, which also showed expansile pulsation and a thrill and was supplied by a very large artery, approximately 2 cm in diameter   During the course of the operation the right middle lobe bronchus was wounded and it was therefore necessary to remove both the right lower and middle lobes   This was very difficult, partially because of the multiple vascular adhesions to the chest wall and diaphragm and partially due to the incomplete interlobar fissures, and as a result there was considerable blood loss   Before the removal of the tumour the patient's condition was poor, his systolic blood pressure was between 70 and 80 and was not improved either by transfusion or by bronchoscopic clearance of his normal lung   However, after right and middle lobes had been successfully removed he partially recovered, his blood pressure rising to 85/50 and his cyanosis disappearing   The operation lasted five hours, and during this period he received 3 pints of plasma and 1 5 pints of blood

On returning to the ward his condition failed to improve, although his colour remained good and there was now no evidence of cyanosis, his systolic blood pressure did not rise above 90, his respirations were shallow, bubbling and stertorous and he was deeply unconscious   X-ray of his chest showed complete collapse of his right upper lobe and on bronchoscopy a few ml of mucoid material were aspirated   In spite of a transient improvement with this measure he lapsed into deeper coma and died some thirty hours after operation

Necropsy was done by Dr F Camps, on April 7, 1948, twenty-three hours after death   There was about 250 ml of free fluid blood in the right pleural cavity and a slight extravasation into the posterior mediastinium   The remaining upper right lobe contained no air but some lymph deposits   The left lung was moderately well ærated, deeply congested, with peripheral collapse of the lower lobe where there was also a small hæmangioma   Subpleural and pericardial hæmorrhages were seen The heart was normal with some right sided dilatation   There was gross distension of the veins of the liver but no angiomata   The kidneys were also congested with dilated veins

The specimen removed at operation is shown in Fig 5 and is reported on by Dr Allanby   "The specimen consists of the right middle and lower lobes   The pleura is wrinkled due to partial collapse of the lobes, but bears no sign of inflammation   The lateral pleural surface of the lower lobe shows patches of calcification, more easily felt than seen   Some fibrous adhesions are seen upon the diaphragmatic surface   The pulmonary vein leaving the lower lobe is grossly dilated and appears to communicate with a large thin-walled loculated system of spaces   The cut surface of the lower lobe shows a multilocular hæmangioma in its substance, measuring 3 5 cm by 3 0 cm adjacent to the calcified pleura, and 4 cm from the main lower lobe bronchus   A branch of the pulmonary artery communicates directly with this cavernous space without capillary intervention   The surrounding lung and the middle lobe are normal   Sections showed the typical microscopic appearances of a cavernous hæmangioma '

THE SECOND CASE

J A , aged 13, was admitted to Guy's Hospital in September 1948 with acute osteomyelitis in the middle of the shaft of the left femur, this was associated with a positive blood culture and quickly responded to treatment with penicillin   Cyanosis was noticed at 5 years and had progressed to a degree when it was obvious at rest, with marked clubbing of the fingers and toes   He had early been diagnosed as congenital heart disease and attended a special school, to which he was driven by ambulance, once there, he played football without any distress Both parents and their three other children were normal   A provisional diagnosis of arteriovenous aneurysm of the lung as the cause of his cyanosis was made on admission by the registrar, Dr W D Brinton, on the X-ray appearance of the lung (Fig 6A) and was confirmed by the finding of a continuous murmur in the left upper chest as soon

BRONCHUS

PULM ARTERY

GROSSLY DILATED PULM VEIN

CALCIFICATION OF PLEURA

DIAPHRAGMATIC SURFACE
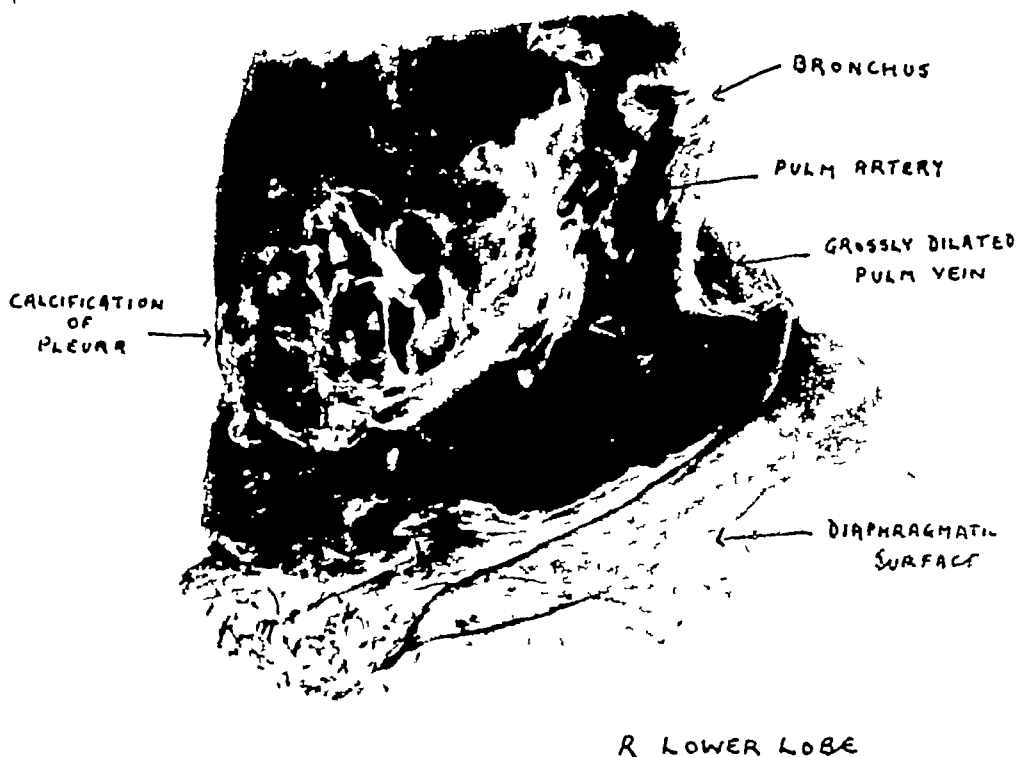
R LOWER LOBE

Fig 5 —Case 1   Cut surface of lower lobe removed at operation

as the pulse slowed, and subsequently by angio-cardiogram (Fig 6B)

He was a boy of average height for his age, but spare   Cyanosis was obvious at rest, with some suffusion of the conjunctivæ, and was increased by exercise, though he was not unduly breathless Clubbing was marked   He did not squat when tired   The heart was not enlarged clinically and on X-ray showed a prominent pulmonary conus only and a cardio-thoracic ratio of 10/23 cm   There was a short systolic murmur in the first and second left spaces 2 to 3 in from the midline and an increased pulmonary second sound   Apart from this, heard over a wide area but best appreciated 10 cm from the midline in the second space, was a more distant but clear continuous murmur, which could just be heard in the back above the left scapula   there was no thrill   The blood pressure was 115/75   Careful search found no systemic angiomata   The hæmoglobin was 126, with 7 2

million red cells and a colour index of 0 88   The electrocardiogram (Fig 8) showed no right axis deviation   The appearance on straight X-ray was of a mottled opacity in the apical and subapical segments of the upper left lobe composed of rather worm-like streaks tending to radiate upwards and outwards from the hilum   That these were vascular shadows was clearly shown on angiocardiography where most of the dye was shunted through the opacity, the arterial elements being filled in two seconds and the larger venous channels in the third second   At the moment of reporting this case, for which we are indebted to Dr Hampson, Mr Brock has agreed to operate, but this has not yet been done *

DISCUSSION

It will be seen that these two cases present a clear-cut clinical picture, but it is only of recent years that

* Mr Brock successfully removed the left upper lobe containing the arteriovenous aneurysm on February 10 1949 there was a large collateral circulation from the bronchial arteries   Following operation cyanosis has disappeared and his physical capacity has increased

A   B
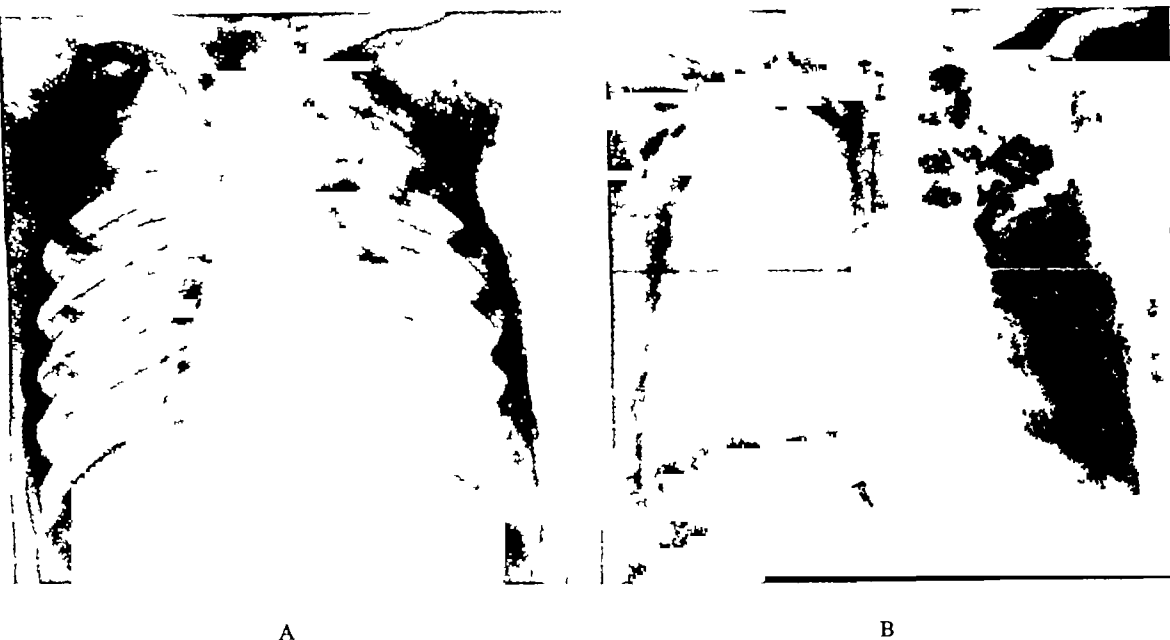
FIG 6—Case 2, aged 13 (A) Straight X-ray showing streaky radiating shadows in left upper lobe (B) Angio-cardiogram at 2 sec from injection of dye, showing the vascular nature of the shadow in the left upper lobe

it has been recognized In 1936 Bowers reported a fatal case in a child of two days old, and in 1938 Rodes described the clinical picture in an adult The first reported case treated surgically was in 1942 by Hepburn and Dauphinee, where the aneurysm was removed and the condition cured We have found 29 cases so far reported and although they are not all described in full detail a reasonable survey can be made, to which we are adding these 2 further cases

With the exception of the case of Bowers (1936), one mentioned by Sweet in the discussion following Maier's (1948) paper, and our second case, the diagnosis has been made in adults, the average age of 26 cases being 29, with extremes of 16 and 51 Nevertheless it appears that the condition has in most cases been present in childhood, for in 15 cases where the onset of cyanosis is given, it is since birth or early childhood in 8, between the ages of 6 and 14 in 4, and in only 3 is it stated to have begun in adult life Both sexes are affected but in the reported cases there is a predominance of males A family history has been suggested in five instances, of which two seem certain, and Goldman s two cases of arterio-venous aneurysm in the lung (1943 and 1947) were brothers

Cyanosis is the most important feature and its absence was noted in only two cases, that of Duvoir and Picot (1939) who had many visceral angiomata

and died of pneumonia aged 16, and Whitaker s (1947) second case, aged 33, where there was no disability, Maier (1948) makes no mention of this point in his case It is only in these three that absence of " clubbing " is specifically mentioned, and with a few exceptions where no note is made it is, as might be expected, a feature that goes hand in hand with the degree of cyanosis Pulmonary osteo-arthropathy is reported once by Adams (1944) Polycythæmia in the cyanosed cases is a constant finding with an average of 7 3 million in red cells, the highest figure being 11 4 million in Goldman s (1943) case, the colour index tends to be low, a common finding in polycythæmia It is likely, however, that although cyanosis is almost a constant finding in reported cases, both the increasing recognition of this condition and the increase in routine X-rays of the chest will reveal earlier cases before cyanosis develops

It is not surprising that the combination of cyanosis, clubbing, and polycythæmia usually occurring from an early age, often suggests a diagnosis of congenital heart disease, noteworthy exceptions to this misdiagnosis being Smith and Horton's (1939) and Goldman's (1947) cases, both in adults, who had been under treatment for poly-cythæmia rubra vera Nothing, however, is found amiss with the heart either on clinical or radiological examination, the sole abnormalities recorded being
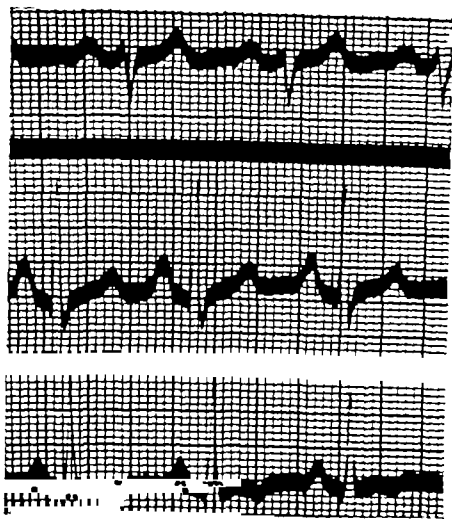
FIG 7—Case 1   Standard leads showing marked right axis deviation with large P waves and inverted T III
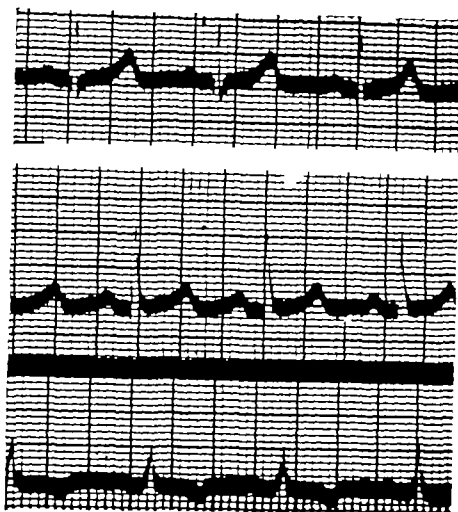
FIG 8—Case 2   Standard leads showing no right axis deviation

by Sisson *et al* (1945) with a systolic murmur and enlargement, by Alexander (1945) with enlargement to the left without a murmur, and by Lindgren (1946) whose second case had mitral stenosis   Nor, with the possible exception of Sisson's (1945) case, is there any history of these cases developing heart failure, and though congestive failure was suspected in our first case the cardiac catheterization showed that this was not present   That arteriovenous shunts in the lesser circulation produce so little effect on the heart is in marked contrast to the well recognized strain exerted when similar shunts occur in the systemic circulation   It would, therefore, seem that the combination of cyanosis, clubbing, and polycythæmia, with normal findings on examination of the heart, should suggest the possibility and search for arteriovenous aneurysm of the lung

The main symptom of the condition is dyspnœa which has not preceded the cyanosis in any patient   The degree of disability in many has been slight, particularly considering the degree of cyanosis, and in only 7 of the 29 reported cases would it appear to have been marked   In this respect our first patient appears to have been an unusually severe and late example of the condition   Attacks of dizziness and faintness, not amounting to loss of consciousness, such as were experienced in our first case, have been noted in others   They are presumably due to the increased blood viscosity in polycythæmia and are similar to the attacks so common in morbus cœruleus, though cerebral

thrombosis has not occurred   Alexander (1945), however, reports a case of a patient with marked polycythæmia who died of coronary thrombosis   Epistaxis is not uncommon and occurred frequently in our first patient, once necessitating admission to hospital   This is not unusual in subjects of polycythæmia from any cause, but might well be due, in this particular condition, to angiomata in the nasal mucosa, unfortunately we omitted to examine this site, either in life or post-mortem   Hæmoptysis is reported, and was the cause of death in Rodes (1938) case, and Lindgren's (1946) third case had been diagnosed and treated as pulmonary tuberculosis on account of this symptom

In contrast to the negative findings on clinical examination of the heart, a murmur in the lungs, usually systolic but occasionally with a diastolic component, was found in 14 of 23 cases where this sign is mentioned   Similarly in 19 cases where the point is made, associated lesions in other parts were found in 12, the commonest site being on the lips   These two signs, therefore, afforded strong confirmatory evidence of the diagnosis of arteriovenous aneurysm of the lung

The clinical diagnosis is confirmed by radiology and in no case has a straight X-ray failed to show the lesion in the lung   No doubt in many instances, as in ours, the finding of a shadow away from the heart has been the finger pointing to the answer in a puzzling clinical problem   These are variously described as rounded, with defined or with irregular edges, wormlike, or as an extension of the hilar

vascular pattern pulsation may be seen and calcification had developed in our first case Tomography will clarify and localize, and kymography may show pulsation not visible or established by cardioscopy, but the angiocardiogram is most helpful not only in establishing the vascular nature of a doubtful shadow but in outlining aneurysms close to the mediastinum or hilum or obscured by the heart Though the experience of Sisson *et al* (1945) whose case died as a result of this investigation, must be remembered an angiocardiogram was amply rewarded in our first case by showing two additional shadows not seen on the straight X-rays or on screening As multiple shadows have occurred in about half the cases, this investigation would appear to be necessary if surgical intervention is contemplated

Investigations of the circulatory dynamics have not been common The circulation time in our first case was normal, which is in accordance with the findings of Makler and Zion (1946) and of Watson (1947) The percentage of blood passing through the shunt was estimated by Maier (1948) to be 58, compared with 25 to 30 in one of Lindgren s (1946) cases and the 80 in our first case Normal intracardiac pressures were found on catheterization in our case as in Maier's (1948) but unlike our very high figure of 10 to 20 litres a minute, the cardiac output was normal The increased blood volume which we record was found in all the 8 other estimations made It is due to the increased cell volume, the plasma volume being unaffected, a distinction from arteriovenous aneurysms in the systemic circulation where both cell and plasma volume are increased with a normal haematocrit reading

The natural course and prognosis of a condition so recently recognized and so readily subjected to surgery is not easy to estimate From the reported cases it is clear that there is steady, though often slow progression from cyanosis alone, the first sign of a lesion of any size, to symptoms of breathlessness, to restricted activity, and in a few cases to complete disability It must be remembered that cyanosis alone is disfiguring in the developing child or young adult and there are associated hazards from vascular accidents due to the polycythæmia or the lesion itself In the 29 cases we have found, 5 died one from a hæmoptysis at 25 (Rodes), one aged two days from hæmorrhage through the pleura (Bowers), one from coronary thrombosis at 41 (Alexander), one case, not cyanosed, from pneumonia at 16 (Duvoir), and one aged 45, a severe case, as the result of angiocardiography (Sisson) While the average age of the group is 29, and many had little disability except the cyanosis —notably Smith and Horton's case of a " blue

baby ' who at 46 had only some dyspnœa — there is no case older than 51 It would therefore appear that in those with lesions of any size, where cyanosis is of necessity present, the expectation of life is diminished, though up to the age of 30 the hazards are not great This would suggest that in these, operation, if it is a reasonable risk, should certainly be contemplated, for if successful, it would mean a cure

Even allowing for unsuccessful cases which might not so readily be reported, the results are certainly encouraging Five of the cases died and 19 of the remaining 24 cases had operations There were 2 fatalities, to which we now add another In one where the operation is not described, the disappearance of cyanosis is noted as slow, but the others—three with local excision, the remainder with lobectomy or pneumonectomy—are reported as cures although post-operative observations are minimal and follow-up necessarily short In arteriovenous aneurysm of the lung where cyanosis is present it would seem therefore that operation is not only indicated but is a reasonable risk We know that children stand thoracic operations better than adults so that it is important to make the diagnosis at an early age In those where the condition is recognized without cyanosis—and the quickening appreciation of it will probably reveal cases where an obscure lung shadow is the only finding—the need for surgical intervention would appear small Whitaker s second patient who refused operation was one of these, and it is by following these types of cases that we shall get a wider appreciation of the natural course of a condition, possibly by no means rare, which so far has been diagnosed only in its more severe degrees

SUMMARY

Two cases of arteriovenous aneurysm of the lung are described and discussed with 29 cases previously reported A clear clinical picture, which has only been recognized in the last ten years, is seen, and the condition is by no means rare Cyanosis from childhood or early adult life, with clubbing and polycythæmia are the most important features Physical signs in the heart are uncommon but a murmur may be heard in the chest, corresponding to the invariable finding of an opacity in X-ray of the lungs Associated vascular lesions in skin, mucous membranes, and particularly the lips are common The cyanosis is slowly progressive and is followed by dyspnœa, restricted activity, and eventually incapacity Hazards to life are from anoxæmia, polycythæmia, and hæmorrhage from the aneurysm, rather than from heart failure The

commonest misdiagnosis is congenital heart disease when cyanosis develops in early life, as is common, but it may also be mistaken for polycythæmia rubra vera if cyanosis first develops in adult life, or pulmonary tuberculosis when hæmoptysis occurs with the undiagnosed X-ray opacity

It is successfully treated by removal of the aneurysm, by lobectomy or pneumonectomy

Surgery is a reasonable risk and indicated in those with lesions large enough to cause cyanosis The importance of early diagnosis and surgical intervention at an appropriate stage in the disease is stressed

We are indebted to the numerous colleagues at Guy's Hospital, mentioned above who co-operated in the investigation and treatment of these two cases

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THE HEART RATE WITH EXERCISE IN
PATIENTS WITH AURICULAR FIBRILLATION

BY

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In a previous article (Knox, 1940) an accurate method of recording the changes in heart rate during exercise was described, and results were given for normal subjects performing a brief light step-test This technique has now been applied to patients with auricular fibrillation The present series consists of twenty-two tracings from thirteen ambulant patients with fibrillation

The standard exercise was five ascents of two steps each ten inches high, the rate of stepping being 96 a minute The exercise began and ended in the sitting posture and its total duration was about twenty seconds The heart beats were electrically recorded on a smoked drum throughout exercise and were counted in five-second periods to the nearest tenth of a beat

The clinical condition of the patients with fibrillation was classified as good, fairly good, fair, or poor on the basis of the functional capacity classification of the American Heart Association (1926) This was called the patients' " Exercise Tolerance Group " In addition, the patients were also grouped according to whether they were receiving digitalis or not

Full details of the method of calculating the various heart rate indices were given in the previous article and only a summary need be given here

The *initial rate* is the heart rate averaged over the ten seconds immediately preceding exercise

The *maximum rate* is the highest rate observed during exercise averaged over a five-second period

The *acceleration* of the heart rate is calculated by subtracting the rate in the five seconds immediately preceding exercise from the maximum rate, and dividing the result by the time taken to reach the maximum rate

The *post-exercise rate* is the heart rate averaged over a thirty-second period beginning five seconds after exercise ends

RESULTS

The heart-rate indices The figures for the various heart-rate indices of the fibrillation cases in the different   Exercise Tolerance Groups ' are shown in Table I For comparison, the mean results for 100 normal subjects (75 men and 25 women) are also included in this table It can be seen that there was no correlation between any of these heart rate indices and the patient s clinical condition This was not unexpected, as the number of patients in each group is very small and in addition the completely irregular ventricular rhythm present in fibrillation produces sudden arbitrary changes in heart rate in the successive five-second intervals counted Certain general characteristics, however, can be seen in Table I

Apart from the single case with good tolerance the maximum rates reached during the step-test were much higher than in the normal subjects This was also true for the percentage and actual increases over the initial rates, and for the post-exercise rates

The curve of heart rate during exercise Fig 1 shows the mean curves of heart rate during exercise for the different tolerance groups in all the fibrillation patients who were on digitalis For comparison, the mean curve of the normal subjects is also included in the figure Two of the curves (fairly good and fair) show a distinct *fall* in heart rate during the first five seconds of the exercise, a phenomenon that is of course never seen in normal subjects In general, compared with the normal curve, the acceleration immediately after the beginning of exercise in the digitalized patients with fibrillation is less, but later during the exercise great acceleration occurs, reaching a higher value than in the normals Thus in Fig 1 all the fibrillation curves show a steeper slope in some portion of their course

TABLE I

Index	Mean results in 100 normal subjects	Auricular fibrillation patients grouped by estimate of their exercise tolerance					
		Good	Fairly good	Fair		Poor	
		on digitalis (1 case)	on digitalis (2 cases)	on digitalis (2 cases)	not on digitalis (1 case)	on digitalis (4 cases)	not on digitalis (3 cases)
Initial rate (beats/min)	87	67	116	96	136	100	116
Maximum rate (beats/min)	131	130	185	151	235	155	182
Acceleration of heart rate (beats/min /sec)	2 9	2 3	2 2	2 8	6 0	3 1	2 3
Percentage increase on initial rate	53	95	60	59	78	59	64
Actual increase in beats/min	44	63	69	56	100	56	65
Post exercise rate (beats/min)	93	104	140	132	176	135	165
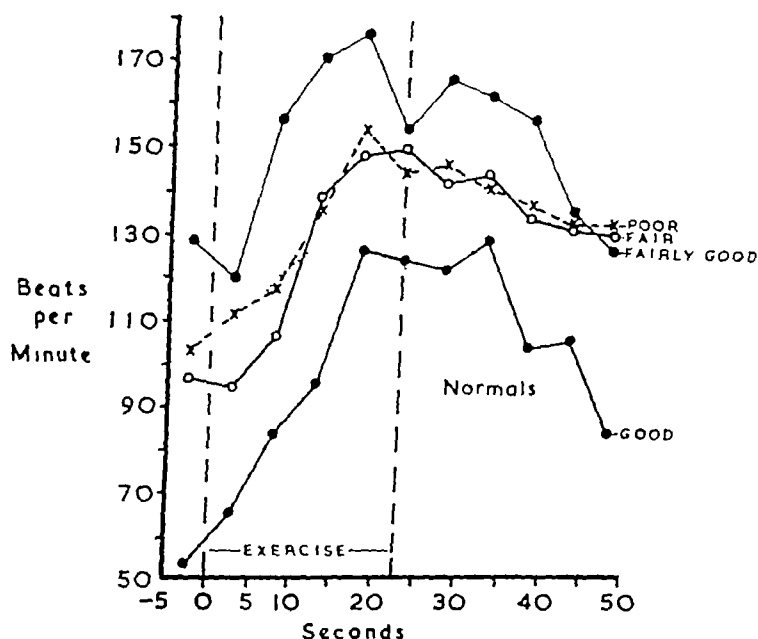
FIG 1 —Auricular fibrillation patients on digitalis (Series C)   Graphs of mean heart rates before, during and after the standard step test in patients classified into their different ' tolerance groups "
The dotted line shows the mean curve for normal subjects
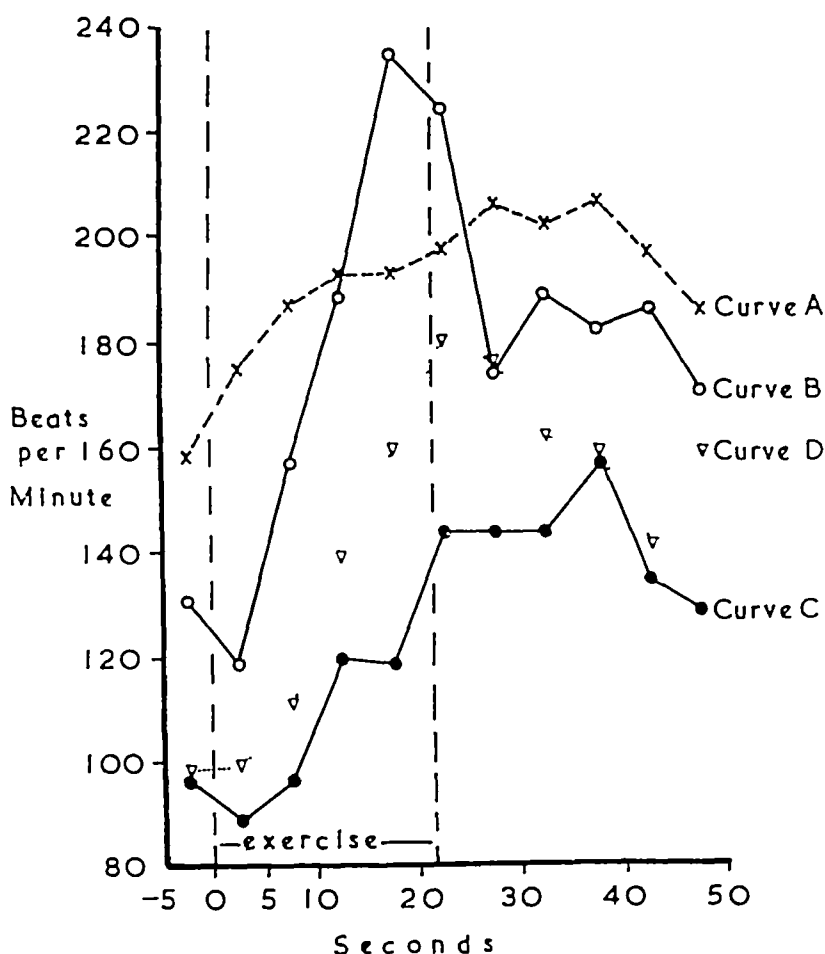
FIG 2 —Auricular fibrillation patients not on digitalis (Series C)   Graphs of heart
rate before, during and after the standard step test in four patients
Curves A, B, C, and D are each from a separate patient

than does the normal curve   This sudden delayed acceleration was very characteristic of those with fibrillation   It will also be seen that after the end of exercise the heart rate falls very slowly compared with the normal, especially in the poorer tolerance groups

The curves of heart rate during the step test in four patients with fibrillation who were not on digitalis are given in Fig 2   In general they show the same characteristics as the digitalized patients, these include the drop in rate at the beginning of exercise (in two cases), the delayed acceleration (in three cases) and the continuation of a high heart rate after the end of exercise   Curve B, from a patient with mitral stenosis and fair tolerance has the highest maximum rate reached by any patient, 235 beats a minute averaged over a five-second

period   A portion of the actual tracing is given in Fig 3   It is surprising that such an extreme frequency was reached during a very mild exercise lasting only twenty seconds in a patient who could get about reasonably well   In both the digitalized and non-digitalized groups the curves of heart rate for the patients with ' poor " tolerance did not as a rule show such high instantaneous values of acceleration as the other tolerance groups

Variations in a single subject   It might be expected that owing to the complete irregularity of the ventricular rate in fibrillation there would be very great variations in the shape of the heart rate curve, even in the same patient on the same day   Fig 4 shows three curves of the response of the heart rate to the standard step test performed at 15 minute intervals by the same patient with fibrillation   The
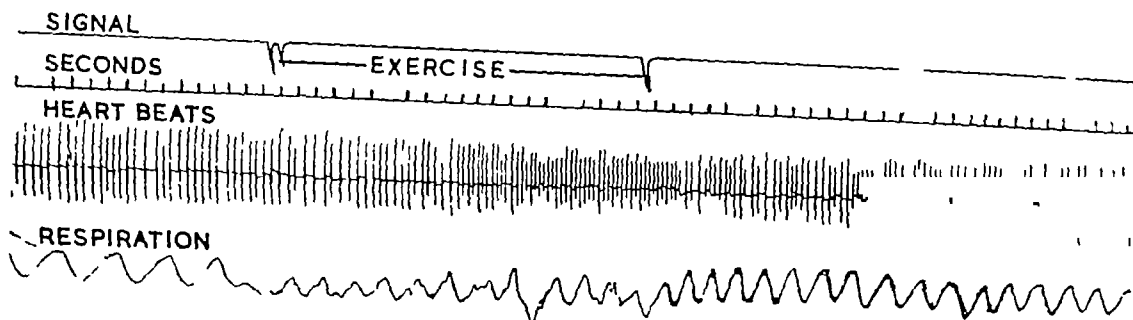
FIG 3 —Kymograph tracing of heart beats from a patient with auricular fibrillation   Between the dips in the signal line the patient performed the standard two-step test   During the last half of exercise the extremely high heart rate of 235 beats a minute was attained

Upper line —signal
Second line —time in seconds

Third line   —heart beats
Fourth line —respiration
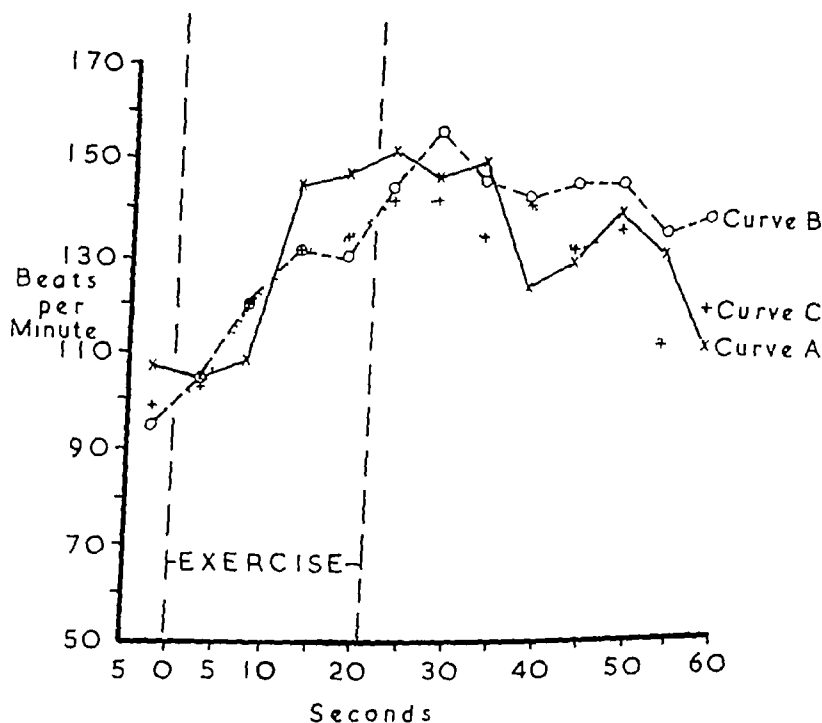
FIG 4 —Effect of repetition of the standard step-test 3 times at 15 minute intervals on the heart rate of a patient with auricular fibrillation (Series C, Case C 49)

Curve A—Heart rate before, during, and after the standard step-test
Curve B—The same, 15 minutes later
Curve C—The same, 15 minutes after Curve B

curves were taken in the order A B C The varia-tion is greater than one would expect from a normal subject, but in view of the complete arrhythmia the general shape of the curve is remarkably well main-tained It can be seen that the acceleration tends to decrease in successive tests Similar results were obtained from two other patients with fibrillation

There was some evidence that this constancy in the shape of the heart rate curve of a given patient may persist over considerable periods of time even when the clinical condition has improved or de-teriorated The curves for two such patients during the standard step test are shown in Fig 5 Curve A is from a patient on digitalis whose tolerance classification was fairly good Curve B is from the same patient one year later when the clinical condition had improved, the dosage of digitalis remaining unchanged Curve C shows the response in another patient with fibrillation also on digitalis His tolerance classification was poor and coupling of the beats was present Curve D is from the same patient six months later when his general

condition had become worse, though the coupling was now absent The figure demonstrates how the characteristic shape of the curve for each patient was maintained even after an interval of many months Thus curves A and B both show a " peak " type of curve with marked oscillations after the end of exercise, whereas curves C and D are of the ' plateau type with a relatively smooth post-exercise fall in rate

The improvement in the condition of the first patient is accompanied by a fall in the general level of his curve, whereas the reverse is true of the second patient whose condition had become worse While this does suggest that the exercise heart rate curves of these patients may vary with their clinical con-dition it is also possible that the variations were due to different degrees of digitalization, although the actual dosage remained constant in each case

The tracing from which curve C was taken showed the actual onset of a period of coupling A repro-duction of part of this tracing is given in Fig 6, and the start of coupling in a burst of extrasystoles can
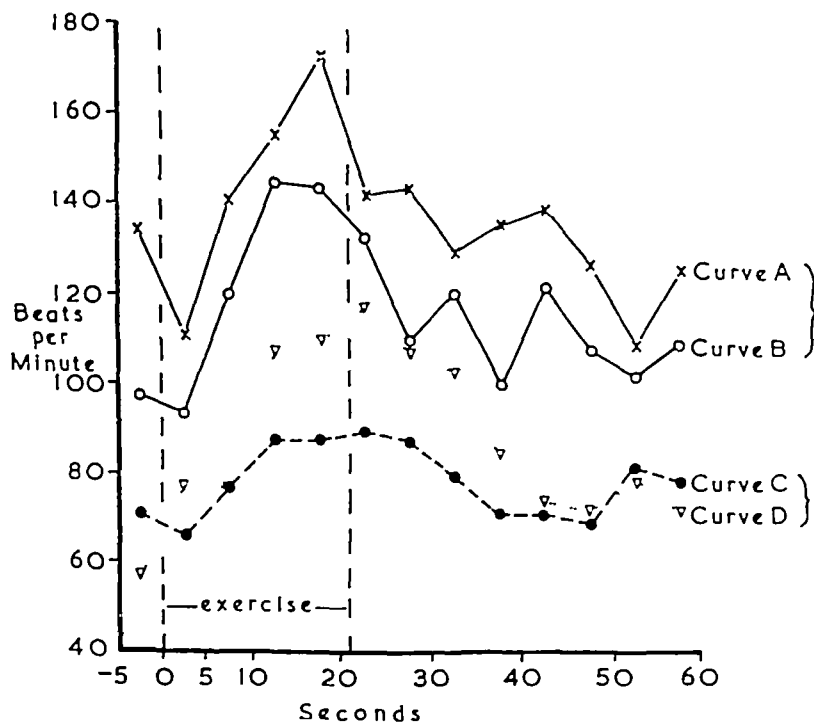
FIG 5 —Curves of heart rate during the standard step-test in two cases of auricular fibrillation
Curve A—Heart rate before, during, and after the step-test
Curve B—The heart rate in the same patient one year later when the clinical condition had improved
Curve C—Heart rate before, during, and after the step-test in another fibrillation patient
Curve D—The heart rate six months later in the same patient as Curve C, when the clinical condition had deteriorated
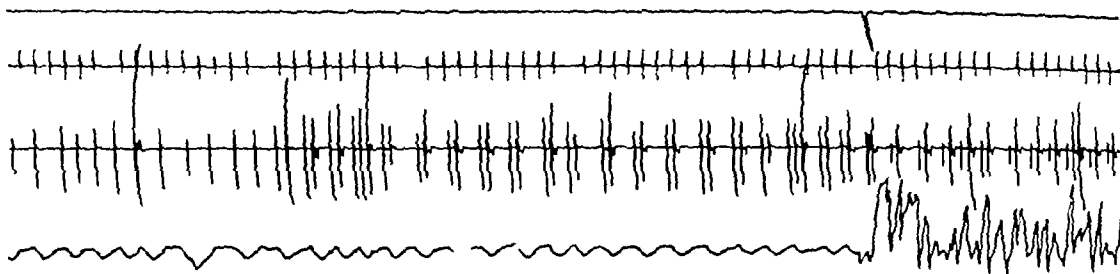
FIG 6 —Kymograph tracing showing onset of a period of coupling in a patient with auricular fibrillation
  The coupled beats begin after a burst of extrasystoles
  The dip in the signal line indicates the beginning of the standard step-test

Upper line —signal   Third line —heart beats
Second line—time in seconds   Fourth line —respiration

be seen to occur about thirty-five seconds before the beginning of exercise   The coupled beats persisted throughout exercise and were still present when the patient left the laboratory some fifteen minutes later   This patient may have been of the type referred to by Goodman and Gilman (1941) in whom relatively small doses of digitalis may cause coupling, as he was receiving only 1 grain tab dig pulv once daily

DISCUSSION

Blumgart (1924) was the first to attempt a quantitative estimate of the effect of exercise on the heart rate in cases of fibrillation   His exercise consisted in stepping twenty times on and off a chair, and the test was carried out by six controls and nine patients   Heart rates were recorded before and immediately after exercise, but no records were obtained during the exercise period   He concluded that fibrillating hearts respond to a given exercise by a disproportionate rise in ventricular rate and by a delayed return to normal   Both these findings are upheld by the present results as can be seen from Fig 1 and 2

Blumgart also found that digitalis in ordinary doses failed to prevent the exaggerated response to exercise, in fact, the actual increase in rate was slightly greater under digitalis   In the present series it was not possible to compare the results in the same patients while on and off digitalis but it can be seen from Table I that the actual increase in heart rate of the digitalized cases was much greater than in the normals so that here also digitalis has failed to protect completely against an exaggerated rise in rate   The actual increase, however, in the non-digitalized patients is on the average consider-

ably greater than in patients of the same tolerance group who were receiving the drug   In general, if we consider the patients in the " poor tolerance " group of whom four were on digitalis while three were not, all the indices except the acceleration of the heart rate are higher in the non digitalized group   Digitalis, therefore, while failing to abolish the exaggerated increase in rate, did appear to diminish it to a considerable extent in my cases *   Although contrary to Blumgart's findings, this is in agreement with the results of Weinstein, Plaut, and Katz (1940) who showed that digitalis when used in large therapeutic doses lessened the ventricular acceleration due to a standard exercise test in ambulant fibrillation cases

This is of interest in connection with the work of Gold et al (1939) who analysed the relative importance of the vagal and extra-vagal mechanisms by which digitalis slows the ventricle in fibrillation   They found the slowing caused by small doses of digitalis (up to about 60 per cent of the full dose) could be counteracted by large doses of atropine, so that it was largely due to vagal stimulation   When full doses of digitalis were given, atropine could no longer increase the ventricular rate and the slowing was then clearly due to extravagal actions of digitalis   The main extravagal action was said to be the increase in the refractory period of the A V conduction system

In 1941 Modell, Gold, and Rothendler applied these results to the exercise acceleration of the ventricle in patients with fibrillation   They concluded that in the average case the exaggerated acceleration during exercise was due chiefly, if not entirely, to decrease in vagal tone, and that blocking the vagus by atropine accelerated the ventricles to the same maximum level as extreme physical

* Dr Maurice Campbell informs me that he (and no doubt other cardiologists) have been in the habit of teaching for years that the amount of digitalis needed for satisfactory control for a patient at rest in hospital is smaller than the amount often needed to control his heart rate when he is doing more and getting about outside the hospital   This fits in well with the experimental points

exertion Extra-vagal digitalization with large doses prevented the exaggerated response to exercise through direct action on the A-V conducting system, in accordance with the theory They also pointed out that the ventricular rate at rest does not indicate whether digitalis has caused slowing by the vagal or the extra-vagal mechanism, but that there are two simple ways of detecting extra-vagal digitalization Either 2 mg of atropine may be given intravenously or the patient may be made to exercise If neither of these procedures raises the ventricular rate to over 100 a minute, then enough digitalis has been given to cause slowing by the extra-vagal mechanism Judged by the latter test, the extra-vagal mechanism can only have been prominent in one of the digitalized cases of the present series and there it was associated with marked coupling of beats It is noteworthy that this was the only case in which no delayed acceleration of the heart occurred and it is thus probable that a sudden diminution in vagal tone was the main factor causing the delayed acceleration

SUMMARY

In a series of thirteen ambulant patients with fibrillation the maximum heart rates reached during a short standard step-test were much higher than in normal subjects

No correlation was found between any of the heart-rate indices (initial rate, maximum rate, acceleration, percentage increase, actual increase, and post-exercise rate) and the clinical condition of the various patients

In spite of the complete irregularity of the ventricular rate, the response to exercise in a given patient was reasonably constant

In some cases a brief fall in heart rate occurred at the beginning of exercise

An almost constant feature was a sudden delayed acceleration of the heart rate commencing about twelve seconds after exercise had begun

Digitalis, while failing to abolish the exaggerated increase in rate, appeared to diminish it to a considerable extent

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CALCIFIED AORTIC VALVE

CLINICAL AND RADIOLOGICAL FEATURES

BY

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The object of this paper is to suggest that a diagnosis of calcified aortic valve can justifiably be made more often than is the current practice, and that the lesion can be convincingly demonstrated and permanently recorded by a special radiological technique not hitherto described

Rayger described the first recorded case of calcified aortic valve in 1697 he performed an autopsy, and sent one of the calcified cusps to Bonet, who described it in a publication dated 1700 A few years later Cowper (1706) described a man of forty with dyspnœa, angina, faintness and petrifaction of the aortic valve—" the valves of the Great Artery were Petrify'd insomuch that they could not approach each other " Further cases were reported by Vieussens (1715), Chevers (1842), Lloyd (1846), and Peacock (1868) Lannaec (1829) gives an excellent clinical description The earliest extensive pathological account is that of Hasse (1846)

In more modern times, calcified aortic valve was neglected until 1931, when Christian reported a series of 22 cases, and attempted to lay down clinical criteria for the diagnosis Interest was further aroused by the paper of Sosman and Wosika (1933) on radiological demonstration of valvular calcification, and there have been numerous American papers on all aspects of the subject up to the present time

The English papers on the subject, however, are extremely scanty Bennett (1930) reported a single case, and Gibbs (1935) described the pathology Campbell and Shackle (1932) give the lesion passing mention in a general survey of aortic disease The fullest account written in this country was that of Campbell (1937)

Frequency of the lesion Hall and Ichioka (1940) found 31 cases of calcified aortic valve in 4000 autopsies Dry and Willius (1939) found 23 cases in 2616 consecutive autopsies, and they further pointed out that calcified aortic valve constitutes 18 per cent

of *all* healed valvular defects The highest incidence of the lesion was that reported by Sophian (1945) who found 31 cases in 500 consecutive autopsies at the U S Marine Hospital He attributed the high incidence of the lesion in his cases to age, sex, and occupation Thus it appears that, although the available figures show a fairly wide range of variation, the lesion is undoubtedly quite common

While discussing the incidence of the lesion, it is interesting to note how infrequently aortic stenosis occurs *without* calcification of the valve cusps In Christian's series (1931) of 22 cases there was calcification in all but one, Dry and Willius (1939) reported 116 cases that came to necropsy, in all of which calcification was found, and 122 cases diagnosed clinically with radiologically demonstrable calcification This shows that calcification occurs early in aortic stenosis and is almost always present by the time of death or diagnosis

Unfortunately there are few figures available to show how frequently calcified aortic valve is diagnosed in life Blackford and Bryan (1936) found less than 50 reported cases, that had been diagnosed in life, up to 1936 Berk and Dinnerstein (1938) reported 16 cases, of which only 5 were diagnosed in life, while Reich (1945) reported 22 cases, of which 11 were diagnosed The later series show a much greater frequency of diagnosis than those prior to 1932 e g Margolis *et al* (1931) reported 42 cases, of which only 2 were correctly diagnosed in life

THE MATERIAL FOR THIS STUDY

This paper describes 14 patients suffering from " pure " calcified aortic valve, in whom the lesion was suspected clinically and proved on radiological grounds The table records the main facts concerning the patients

Of the 14 patients, 12 were men and 2 women Their ages ranged from 27 to 71, the average being a little over 50 Only 4 of the patients gave a

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TABLE I

ANALYSIS OF FOURTEEN CASES OF CALCIFIED AORTIC VALVE

Clinical Analysis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Case number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Age	50	62	53	58	53	60	35	46	41	61	43	71	49	27
Sex	M	M	M	F	M	M	M	M	M	M	M	F	M	M
History of acute rheumatism	0	0	0	0	—	±	0	0	0	0	?	0	—	0
Cardiovascular symptoms	0	±	±	—	0	±	—	0	±	±	±	—	—	0
Dyspnœa	0	0	±	—	0	±	±	0	—	—	—	—	—	0
Angina	0	±	±	—	0	—	0	0	—	—	—	0	—	0
Syncope or dizziness	—	+	0	0	0	0	0	0	±	—	—	0	—	0
Œdema	0	0	0	0	0	0	±	0	0	0	0	0	0	0
Clinical cardiac enlargement	0	—	0	—	0	—	±	0	—	0	—	0	±	0
Anacrotic pulse	0	0	0	0	0	0	0	—	0	0	—	0	±	0
Blood pressure (mm Hg)	130	130	110	120	140	200	130	155	120	150	120	150	100	135
	100	95	80	90	85	85	100	85	80	115	90	95	80	80
Pulse pressure (mm Hg)	30	35	30	30	55	115	30	70	40	35	30	55	20	55
Thrill	0	0	—	0	0	—	—	—	—	0	—	—	—	—
Systolic murmur	—	±	±	—	—	—	—	+	—	—	—	—	—	—
Propagation of murmur to neck	+	+	—	—	±	—	—	±	—	—	—	—	—	—
Propagation to whole præcordium	—	0	0	0	—	0	—	—	0	—	0	—	—	—
Aortic second sound	0	0	0	0	±	0	0	0	0	0	0	0	—	—
Aortic diastolic murmur	0	0	0	0	—	0	—	0	0	—	—	0	—	—
Evidence of congestive failure	0	0	0	0	0	0	—	0	0	0	0	0	0	0
Left axis shift or L V strain	0	±	0	±	0	—	—	—	—	—	—	—	—	—
Wassermann reaction	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Peripheral arteriosclerosis	0	±	0	—	0	±	0	0	0	—	0	—	0	0

X-ray Analysis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Heart size	0	±	0	±	±	±	—	±	±	—	—	—	0	—
Calcification visible on screen	—	0	±	0	0	?—	?—	0	±	—	—	—	0	?—
Calcification visible on overpenetrating X-ray	±	0	—	0	0	0	0	0	0	±	0	—	0	0
Calcification visible on tomogram	±	±	±	—	+	±	±	±	—	±	—	—	—	—

history of acute rheumatism, and in one of these it was doubtful None of the patients gave a history of syphilis, and the Wassermann reaction was negative in all cases

The symptoms of which the patients complained varied Four had no symptoms referable to the cardiovascular system of the other 10, 9 complained of dyspnœa, 8 of angina pectoris, 6 of syncope or dizziness, and 1 of œdema One man complained of loss of memory and of the power of concentration

The physical findings were as follows clinical evidence of cardiac enlargement was present in 8 patients, peripheral arteriosclerosis was found in 5, and the pulse was thought to be anacrotic in 4 The blood pressure was not characteristic, but in general the systolic pressure was rather low and the diastolic rather high, unless the former were modified by associated hypertension or the latter by aortic regurgitation The pulse pressure ranged from 30 to 115 mm Hg, the average being 45 mm (see Table) In 9 of the patients there was a basal systolic thrill, and in all 14 a basal systolic murmur The basal murmur was maximal in the second right intercostal space and was propagated to the root of the neck in all cases in 8 of the patients the murmur was audible over the whole præcordium The aortic second sound was audible in only 3 of the cases There was an aortic diastolic murmur in 6 cases but the presence of such a murmur did not bear any significant relationship to the height of the pulse pressure (see Table) Electrocardiography proved of no assistance in diagnosis and showed no characteristic features 11 patients showed evidence of left axis deviation or left ventricular strain, and of these one showed left bundle branch block, one 2 1 A-V block and one the typical changes of anterior coronary occlusion The cardiographs of the 3 remaining patients showed no abnormality

Ten of the patients have been followed up for periods up to two years One died of congestive cardiac failure soon after admission, and 3 died suddenly within a few months of discharge from hospital of the other 6 patients with whom contact has been maintained, one has developed severe dyspnœa and angina pectoris, the other 5 have remained unchanged

ÆTIOLOGY

The ætiology of this condition is uncertain, and this investigation adds nothing to our knowledge of the subject There is no evidence that the lesion is due to a disturbance of calcium metabolism (Bramwell and King, 1942) to focal sepsis as suggested by Thalheimer (1922) or to syphilis (Christian, 1931, Margolis *et al*, 1931, Grant, 1933) Libman (1913) and Perry (1936) observed that subacute bacterial endocarditis may heal by calcification, and Cohen *et al* (1940) described one case of calcified aortic valve that showed healed aneurysms of the hepatic artery with renal and splenic infarcts But, in general, there is no history in these patients suggestive of bacterial endocarditis

The two views most commonly held regarding the ætiology are that it is a form of atherosclerosis (Monckeberg, 1904, Sohval and Gross, 1936), or that it is an unusual manifestation of rheumatic carditis (Cabot, 1926, Karsner and Koletsky, 1940 and 1947, Hall and Ichioka, 1940) Allbutt (1898) first pointed out the low incidence of atheroma of the aorta in cases of calcified aortic valve, and this fact has been confirmed many times since (Clawson *et al*, 1926, Scherf, 1938), Dry and Willius (1939) make a further observation that coronary atheroma is usually in inverse proportion to the degree of aortic stenosis

The incidence of a history of acute rheumatism or chorea in this condition is variable, the lowest incidence (4 per cent) being in the series of Friedwald and Ewing (1938), and the highest (56 per cent) in that of Cabot (1926) In the present series 4 patients (28 per cent) gave a history of acute rheumatism

The sex distribution of the disease is remarkable, whatever the ætiology In favour of a rheumatic origin it has been argued that chorea, which is predominantly a disease of women, is rarely followed by aortic valve disease (Contratto and Levine, 1937, Clawson *et al*, 1938), that rheumatic carditis is a less severe disease in men than in women, and that the mild attacks are most likely to pass undiagnosed, and to be followed by slowly progressive lesions of the aortic valve (Dry and Willius, 1939)

The age incidence is more suggestive of atheroma than of rheumatic valvular disease but cases have been recorded in young persons, and the fact that the lesion is well tolerated may lead to its escaping detection

Histological evidence has been of little value in elucidating the problem, chiefly because authorities disagree in regard to the criteria of what constitutes evidence of old rheumatic affection

The only conclusion warranted by the evidence available is that some patients with calcified aortic valve have, in addition, rheumatic lesions in the mitral valve, that in many cases of calcified aortic valve, without mitral valve disease, there is a history of acute rheumatism, and that those patients without mitral disease or a history of acute rheumatism, have lesions in the aortic valve that are indistinguishable from those in the other two groups

CLINICAL SYMPTOMS

Age and sex In general the disease is one of men past middle life (Fothergill, 1879) The average age varies in different series from 52 years (Contratto and Levine, 1937) to 60 years (Friedwald and Ewing, 1938) The youngest case on record was a boy of 12 (Gautier, 1860)

The predominance of males is very striking With the exception of Margolis *et al* (1931), in whose series only 21 per cent were males, most series show a male incidence of over 80 per cent This feature of the disease is difficult to explain The suggestion that the more arduous physical life of the male, subjects the aortic cusps to greater trauma is not convincing It seems more likely that the explanation lies in a difference in the natural history of acute rheumatism in the sexes

Symptoms Trousseau (1870) commented on the disparity between the mildness of symptoms and the severity of this lesion as demonstrated at autopsy In this present series 3 of the 14 patients had no symptoms referable to the cardiovascular system

Dyspnœa This was the commonest symptom, occurring in 11 of the 14 cases, 2 (Cases 4 and 7) complained of dyspnœa at rest, the others only on exertion None complained of nocturnal paroxysmal dyspnœa, which is remarkable in view of the burden thrown on the left ventricle by calcified aortic valve

It is remarkable that the lesion may be of long duration and associated with gross cardiac enlargement without producing dyspnœa This may possibly be explained by the slow development of the so-called 'compensatory hypertrophy of the left ventricle over a long period

Angina pectoris The occurrence of angina was recorded in 1706 by Cowper whose patient complained   of pain about the heart' and by Morgagni (1769) The discomfort experienced is

often atypical, conforming rather to the true etymology of the word several of the patients (Cases 10, 11, and 13) denied retrosternal pain but complained of a choking sensation on exertion One man (Case 3) complained of a ' heavy ' pain below the left nipple which was significantly related to exertion In Cabot s series (1926), only 3 of the 9 patients with angina had typical distribution of pain Levine (1945) also noted that the pain was often atypical, and that the history was elicited only by careful questioning

Eight out of 14 patients in the present series (57 per cent) complained of anginal symptoms The incidence of angina in other series varies from 7 per cent (Grant, 1933) to 60 per cent (Friedberg and Sohval, 1939) Case 4 had an attack clinically and cardiographically indistinguishable from coronary thrombosis, she did not die in hospital and no autopsy was obtained Boas (1935) reports a patient with typical symptoms and electrocardiogram of coronary thrombosis, whose coronary arteries at autopsy were healthy, he suggests that the onset of left ventricular failure may simulate coronary thrombosis, as a result of a sudden fall in cardiac output, with reduced coronary flow

The mechanism of angina of effort in this disease is not clear There is rarely associated disease of the coronary arteries or their ostia (Boas, 1935, Reich, 1940, Contratto and Levine, 1937), nor can the occurrence of angina be related to aortic regurgitation Although 3 of the 8 cases with angina had aortic diastolic murmurs, none had the peripheral manifestations of aortic regurgitation

Friedberg and Sohval (1939) suggested that angina was due to the very high intraventricular pressure, which develops in systole with intense contraction of the ventricle, compressing the coronary vessels in a manner comparable to the blanching of the clenched fist Levine (1945) made the ingenious suggestion that angina was due to the forcible ejection of blood into the aorta in systole, causing a suction action and leading to coronary *emptying* But whatever the mechanism of angina may be in this condition, there is no doubt that calcified aortic valve is *the* valvular lesion above all others associated with that symptom, if luetic aortitis, which is not primarily a disease of the valve, be excluded

Dizziness and syncope Cowper s patient (1706) ' complained of great faintness ' and this appears to be one of the commonest and most disabling symptoms of calcified aortic valve Contratto (1940) states that ' dizziness and syncope help to distinguish aortic stenosis from mitral stenosis and aortic incompetence, in which these symptoms are very rare

In the present series 5 patients complained of disturbances of consciousness varying from a transient loss of attention to complete loss of consciousness lasting for some minutes Loss of consciousness was not accompanied by an aura, convulsions, or incontinence, and recovery was complete immediately, without disturbance of memory, speech, or motor power, and without paræsthesiæ or headache Marvin and Sullivan (1935) and Scherf (1938), on the other hand, state that the attacks are sometimes epileptiform in character

In some of our cases the attacks were related to exertion (Cases 1, 2, 9, and 11), a fact observed by Fothergill in 1879, but in others they occurred when the patient was at rest (Cases 10 and 13) Marvin and Sullivan (1935) related the syncopal attacks to exertion in all their 11 cases except 1, in whom the attack was post-prandial

Mechanisms of disturbances of consciousness It seems indisputable that the ultimate cause of loss of consciousness is cerebral anæmia, but the mechanism is obscure Smith (1931) attributed it to insufficient left ventricular output in exertion, through a narrow aortic orifice But in some cases syncope occurs at rest, and the occurrence of syncope is very variable, the amount of exertion which produces syncope one day having no effect on another

There is no evidence that Stokes-Adams attacks are responsible for syncope, as the electrocardiogram between attacks shows evidence of heart block (2 1) in one case only (Case 11) this patient suffered from giddiness only and did not lose consciousness Marvin and Sullivan (1935) induced an attack of syncope by exertion in one of their patients, and took continuous cardiographic tracings At the onset of unconsciousness the heart rate was slow (50 a minute) and regular, the tracing showed nodal rhythm and marked depression of the origin of T II A few seconds later ventricular premature beats appeared followed by simple paroxysmal tachycardia at a rate of 200 a minute There were frequent changes in the position of the pacemaker after the subsidence of tachycardia They concluded that loss of consciousness was due either to carotid sinus hypersensitivity, as described by Baker and Weiss (1935), or to diminished coronary flow during exertion, with a cardiac output so low as to induce unconsciousness Carotid sinus hypersensitivity seems an improbable explanation Contratto and Levine (1937) found that carotid sinus compression produced no effect in 19 patients with calcified aortic valve, who complained of disturbance of consciousness, and that observation has been borne out in the present series (Cases 10, 11, and 13) The most acceptable explanation so far put forward

is the occurrence of reduced coronary circulation with a marked reduction in cardiac output

Mental changes One patient (Case 10) complained of loss of memory and concentration sufficient to interfere with his normal activities

PHYSICAL SIGNS

Blood pressure The systolic blood pressure in the present series ranged from 100 to 200 mm the diastolic from 80 to 115 mm Hg This bears out the findings of Contratto and Levine (1937)

The pulse and pulse pressure Lewis (1934) states " The outstanding feature of aortic stenosis is a small pulse, rising slowly to a delayed summit the condition should never be diagnosed without this sign " Such a view is no longer tenable McGinn and White (1934) found a plateau pulse in only 9 of their 236 cases In the present series the pulse was thought to be characteristically anacrotic in 4 patients only (Cases 7, 10, 11, and 13) in whom the blood pressures were 130/100, 150/115, 120/90, and 100/80 mm Hg respectively In 3 others (Cases 1, 2, and 4) in whom the pulse pressure was 30 mm or less, the pulse was thought *not* to be anacrotic Pulse wave tracings, which might have been of value, were not obtained In the present series the pulse pressure ranged from 30 to 115 mm, the average being approximately 40 mm The pulse pressure presumably depends on the relative degrees of stenosis and regurgitation, and on the presence or absence of associated hypertension

Heart size Levine (1945) states that the heaviest hearts are those with aortic stenosis, although the largest silhouettes on X-ray examination are those with mitral stenosis Christian (1931) found gross clinical cardiac enlargement in all his cases of calcified aortic valve, the average weight at autopsy being 680 g Most authors agree, with the exception of Scherf (1938), who states that " cardiac enlargement does not occur until the lesion has been present for years, often several decades," and Cabot (1926) who found that the heart may be small, moderate, or large

In the present series there was considerable enlargement of the heart in 8 of the 14 cases, slight enlargement in 3, and none in the 3 others In 8 cases the enlargement could be found on clinical examination

Thrill Nine of the 14 cases had a basal systolic thrill Reported cases show great variation in the frequency of thrills in calcified aortic valve Thus Christian (1931) regarded the thrill as an essential criterion, whereas in McGinn and White's series of 123 cases proved at autopsy, 25 per cent had a basal systolic thrill recorded At the other extreme

Gibbs (1935) found a systolic thrill recorded in only 1 of 27 cases It is apparent that the presence of a thrill depends on the intensity of the vibration in the heart, and on the distance of the palpating hand from the source, which may be increased by a thick chest wall or by the presence of emphysema The low incidence of thrill in some of the series discussed from the viewpoint of pathology, such as that of Gibbs (1935), may be due to poor clinical records

The heart sounds Systolic murmur Typically there is a loud systolic murmur, loudest at the base, which is conducted to the root of the neck, more on the right than on the left, and sometimes to the cardiac apex In this series the murmur was harsh and was propagated to the neck in all cases in only 8 cases was it audible over the whole præcordium. In the series of McGinn and White (1934), all 113 cases had basal systolic murmurs, but the authors point out that in some of the cases which came to autopsy a harsh systolic murmur audible over the whole præcordium had, before death, been attributed to mitral valve disease Cabot (1926) found that in 4 of his 28 cases, the systolic murmur was audible *only* at the apex

The murmur is not characteristic (Scherf, 1938), for a similar murmur may be heard in aortic incompetence and in luetic aortitis Nor is its propagation significant, for this depends on the intensity of the murmur (Contratto and Levine, 1937)

Diastolic murmur Lewis (1934) requires an aortic diastolic murmur as well as an anacrotic pulse for the diagnosis of aortic stenosis, but that view is no longer held In the present series an aortic diastolic murmur was heard in 6 out of 14 cases (42 per cent), and this inconstancy of the diastolic murmur is borne out in other series Thus McGinn and White (1934) found diastolic murmurs in 53 per cent of cases, Contratto (1940) in 50 per cent, Cabot (1926) in 57 per cent, and Dry and Willius (1939) in 33 per cent

Aortic second sound On theoretical grounds, it seems unlikely that calcified aortic valve cusps could close with sufficient vigour to produce a second aortic sound In the present series the second sound was inaudible in 11 cases and audible in 3 (Cases 5, 13, and 14), in whom it was of normal intensity Contratto and Levine (1937) suggest that the audible second sound is really a pulmonary second sound Scherf (1938) regards a weak or absent second aortic sound as helpful in distinguishing the murmur of calcified aortic valve from that of luetic aortitis and atheroma of the aorta, in which the sound is normal or accentuated It may be said that whereas the absence of the aortic second

FIG 1 —Case 1   Teleradiograph showing normal heart size and rounding of left cardiac contour, indicating left ventricular hypertrophy

FIG 2 —Oblique radiograph of the heart in the cadaver
   A represents the shadow of a lead strip in the aortic valve area
   B represents the shadow of a lead strip in the mitral valve area

sound favours the diagnosis, its presence does not exclude it

Evidence of congestive cardiac failure   In the present series one patient only (Case 7) presented with signs of congestive heart failure   Other authors have found the incidence much higher, for example, 26 of Cabot's 28 cases presented with œdema

Disturbances of conduction   There have been many reports of disturbances of conduction in this condition   Cowper's case (1706) had ' an intermission of one stroke in three of the pulse," and Parkes-Weber (1897) and Allbutt (1898) described cases with heart block   There have been numerous electrocardiographic reports and an extensive survey by Dry and Willius (1939)   The electrocardiogram is frequently normal   The abnormalities commonly found are left axis shift, T wave inversion, A-V block which may vary in degree in the same patient (Boas, 1935), bundle branch block, smaller degrees of intraventricular block, and, very

rarely, auricular fibrillation (Contratto and Levine, 1937)

Heart block has been attributed to invasion of the conducting tissue by an extension of calcification from the valve (Boas, 1935 and East, 1932)   This may be so in some cases, but it would not account for intraventricular disturbances, nor for variable disturbances   Diminished coronary flow is probably the causative factor in most cases

RADIOLOGICAL COMMENT

Postero-anterior X-rays of the chest in an ' early " case of calcified aortic valve show no evidence of cardiac enlargement   the only change observed is " rounding " of the left lower border of the heart, indicating left ventricular hypertrophy (Fig 1)   The aortic shadow is normal, but a slowly expanding pulsation of the aorta may be seen on the fluorescent screen   In the later stages of the disease, left ventricular enlargement becomes obvious, with increased transverse diameter of the heart
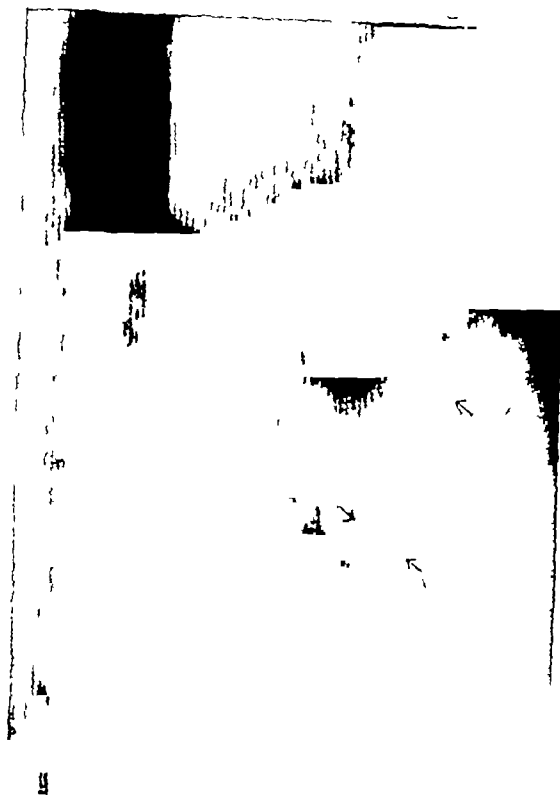
FIG 3 —Oblique tomogram of the heart demonstrating the shadows of calcified mitral and aortic valve The mitral shadow is projected below the aortic one

FIG 4 —Case 1 Oblique tomogram of the heart demonstrating the shadow of a calcified aortic valve

Radiological demonstration of the calcified aortic valve is essential for accurate diagnosis The two methods in common use are fluorescent screen examination and localized overpenetrating X-rays of the heart in oblique positions Intracardiac calcification was demonstrated radiologically for the first time by Klason (1931), who diagnosed a calcified annulus fibrosus on the fluorescent screen but he failed to reproduce it on an X-ray film Saul (1932) was the first to succeed in obtaining a permanent record of a similar case Sosman and Wosika (1933) reported 12 cases of calcified aortic valve, and 13 cases of calcified mitral valve, in which they had observed the intracardiac calcification on the fluorescent screen In their paper a number of important technical points are stressed, among them the need for adequate dark adaptation prior to screening, the use of minimum screen aperture, and examination in the oblique positions Many workers have reported successful application of the technique described by Sosman and Wosika (Parade

and Kuhlman, 1933 Bishop and Roesler 1934 Sparks and Evans, 1934 Sundberg, 1941, and Odquist, 1944)

In the present series demonstration of calcified valves by screen examination or overpenetrating radiographs was not possible in all cases An attempt was therefore made to show the valves by tomography

Tomography was carried out with the patient lying supine in the left posterior oblique position the tube was centred 10 cm below the suprasternal notch in the midline Three or four horizontal "sections were taken at 1 cm intervals above and below an arbitrary plane which experience has shown should be 13 to 14 cm above the table top some of these X-rays inevitably include both aortic and mitral valve areas

The anatomical position of the aortic and mitral valves in X-rays taken in the left posterior oblique position was first ascertained in the cadaver, after lead strips had been placed at the level of the aortic

FIG 5—Case 3   Oblique tomogram of the heart   the calcified aortic valve is demonstrated

and mitral cusps of a normal human heart (Fig 2) Le-Wald (1916) used a similar method to demonstrate the position of the heart valves relative to the anterior thoracic wall

Analysing the shadows cast by calcified heart valves in such tomograms, it is seen that the aortic valve is projected below and dorsal to the level of the pulmonary conus the mitral valve lies below the aortic and roughly in the same plane (Fig 3)

Slight variations in position are common, depending on the size of the heart and associated valvular lesions   Sosman (1934) has discussed these variations extensively, the findings in the present series are similar   If the aortic valve is heavily calcified a clearly defined shadow giving the appearance of a ring is seen (Fig 4 and 5)   In other cases more vaguely outlined shadows are found in the valve area (Fig 6 and 7)

FIG 6—Case 11   Oblique tomogram of the heart demonstrating calcification of the aortic valve
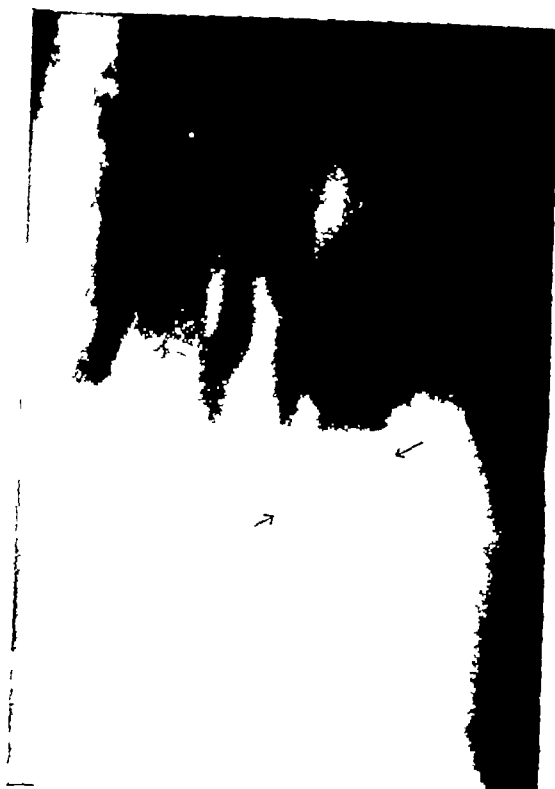
FIG 7—Case 2   Oblique tomogram of the heart demonstrating calcification of the aortic valve   Two separate areas of calcification can be seen

In 6 of the cases reported here, calcification of the aortic valve could be seen clearly on the fluorescent screen in 3 there was a doubtful shadow that could not be identified with certainty in the other 5 cases screening failed to show any evidence of calcified valves   In only 4 cases was reproduction of the calcified shadow on an overpenetrating oblique X-ray possible   Tomography showed the lesion in all 14 cases

It appears, therefore, that tomography is the best method at present available for demonstrating and recording intracardiac calcification

PROGNOSIS

Allbutt (1898) states   ' Aortic stenosis is a long disease, for life may continue under favourable circumstances until the aperture is reduced to the size of a crow-quill or less ''   That point of view still holds today (Scherf, 1938)

The prognosis varies with the age of the patient, and the presence or absence of symptoms at the

time of diagnosis   If discovered in a fairly young person without symptoms, the prognosis is good, the average age at death being 52 (Contratto 1940) If, however, the patient is first seen with symptoms the prognosis is poor, the average expectation of life in the presence of congestive cardiac failure being 9 months (Contratto, 1940) of dyspnœa, 23 months, and of syncope, 9 months (Contratto and Levine, 1937)

In the present series 4 out of 14 are known to be dead   Case 2 died within 6 months of the first attack of syncope, and within 18 months of the onset of angina at the age of 62   Case 4 died at the age of 58, having been known to have a heart murmur for 30 years, and with 5 years history of dyspnœa, and 3 years history of angina   Case 6 died at the age of 60, after one year s mild angina and dyspnœa   he had had acute rheumatism 40 years previously   Case 7 died aged 35, after 6 months dyspnœa of effort, and œdema of the ankles for two days

Causes of death   A certain number of cases die

from causes not connected with the cardiovascular system (as many as 40 per cent in the series of Reich, 1945)

Congestive cardiac failure Congestive cardiac failure is the commonest cause of death it is responsible for about 35 per cent of deaths in the series reported by Grant (1933), by Reich (1945) and by Contratto and Levine (1937) In contrast to mitral stenosis, where the patient may survive several attacks of congestive failure, a patient with failure due to calcified aortic valve rarely recovers (Contratto, 1940) One patient (Case 7) in the present series died of congestive failure after a very short illness

Sudden death After congestive cardiac failure, sudden, unexpected death is the commonest termination It is of interest that the first case recorded (Bonet, 1697) describes sudden death in a Parisian tailor who was apparently in excellent health Many other similar cases have been reported (Lloyd, 1846, Gautier, 1840 Trousseau, 1870 Wilks and Moxon, 1898, Grant, 1933, Lutembacher, 1921) The incidence of sudden death is variably estimated, the average figure being about 18 per cent, although in some series it is very much lower (Campbell and Shackle, 1933), and in others very much higher, as in the selected material of Marvin and Sullivan (1935) In the present series of the four patients who have died in a two year follow-up, three died suddenly

The features and cause of sudden death have been carefully studied by Marvin and Sullivan (1935) They find that death occurs in seconds rather than in minutes, resembling death from coronary thrombosis but no disease of the coronary arteries is usually found at autopsy Nor is the sudden death related to the degree of aortic stenosis They suggest a relation to heart size, pointing out the relative ease with which ventricular fibrillation is induced in large hearts The relation between syncopal attacks and sudden death is not constant, but is sufficiently frequent to suggest that both are

due to a sudden reduction in coronary blood flow with low cardiac output De Veer s suggestion (1938) that sudden death may be due to ' locking of the cusps with complete occlusion of the aortic orifice '' is quite unconvincing

But, whatever the mechanism, sudden death is a frequent event in cases of calcified aortic valve, even though they are symptom-free, and therefore necessitates a guarded prognosis

Other causes of death A few patients have died of superadded subacute bacterial endocarditis (Contratto and Levine, 1937) and a few of coronary thrombosis (Boas, 1935)

SUMMARY

The clinical and radiological features of 14 cases of calcified aortic valve are described, with a method of demonstrating the valves by cardiac tomography

Twelve of the 14 cases were men, 2 were women Their ages ranged from 27 to 71 years, the average being about 50 years Four gave a history of acute rheumatism in the past

The symptoms complained of were dyspnœa, angina, syncope, œdema, and loss of memory, in that order of frequency Four patients had no cardiovascular symptoms

The only constant physical finding was a basal systolic murmur propagated to the root of the neck, other findings were absence of the second aortic sound (11 cases), an aortic systolic thrill (9 cases), an aortic diastolic murmur (6 cases), cardiac enlargement (8 cases), and low pulse pressure (7 cases)

The electrocardiograms of 3 of the patients were normal 11 showed left axis deviation, and of these one showed left bundle branch block, one 2 1 A-V block, and one anterior coronary insufficiency

Four of the 14 patients are known to be dead in a two-year follow up three died suddenly and one in congestive cardiac failure

Tomography was found to be a more successful method of demonstrating calcified valves than screen examination or overpenetrating oblique X-rays

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RIGHT BUNDLE BRANCH BLOCK AND CARDIAC INFARCTION

BY

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It is the object of this paper to investigate the modifications of the electrocardiographic pattern of cardiac infarction caused by the simultaneous presence of right bundle branch block, and to describe the cardiographic signs on which the diagnosis of infarction can be made in the presence of right branch block. The cardiogram of right branch block shows added changes characteristic of infarction, it differs in this respect from that of left branch block which often masks the evidence of infarction

An analysis of tracings taken from patients with right bundle branch block but without infarction will be necessary for the study of cardiograms showing the combined lesion and will, therefore, precede it. All cases under review have the cardiographic pattern of the common variety of right branch block, cases of classical right branch block, characterized by a predominantly downward directed main deflection in lead I, a conspicuous R in lead II, and a tall R in lead III, with T waves in the opposite direction of the main deflection, were not included because of their rarity. A series of twenty-three patients were observed personally, the majority were seen in private practice, and their tracings were taken with a Siemens electrocardiograph, seven patients were seen at the Out-Patient Department of the National Heart Hospital, under Dr

William Evans. A search was made for reported cases to bring the total number of records up to 72

RIGHT BUNDLE BRANCH BLOCK IN HEALTHY SUBJECTS

Right bundle branch block is not rare in healthy subjects and was found 7 times when 1445 healthy persons were examined by Wood, Jeffers and Wolferth (1935). The present analysis is based on 20 cases (see Fig 1 and Table, Cases 1–20). In 7 cases Q deflections were shown in lead I, they were less frequent and never large in lead II. The upstroke of the main deflection and the beginning of the downstroke were slender and steep as in normal curves. The R-T segment showed no significant depression or elevation except for a gradual rise if the following T was high and set close to the QRS complex. The T waves were upright in leads I and II in all cases. The chest lead cardiogram of right branch block, made familiar through the work of Wilson and his collaborators (1934, 1944), was examined in 14 cases, and it included leads from the right præcordial area in 11. Lead CR1 or V1 showed a bifid QRS complex, with two peaks above the isoelectric line, in some records the initial peak was of low voltage (see Fig 1D), there were no Q waves, the R-T segment was either level with the

TABLE OF CASES

No	REFERENCE	CLINICAL DIAGNOSIS
1	Own case	Healthy subject
2	Own case	Retinal arteriosclerosis, normal heart
3	Own case	Healthy subject
4	Own case	Bronchitis
5	Own case	Bronchitis
6	Own case	Healthy subject
7	Own case	Healthy subject
8	Own case	Paget's disease
9	Wilson et al (1934), Fig 1	Cancer of prostate
10	Wilson et al (1934), Fig 2	Pleural effusion
11	Wilson et al (1934) Fig 3	Arthritis
12	von Deesten et al (1934), Fig 1	Dyspepsia

TABLE OF CASES—*continued*

No	Reference	Clinical Diagnosis
13	von Deesten *et al* (1934), Fig 2	Extrasystoles
14	von Deesten *et al* (1934), Fig 3	Healthy subject
15	von Deesten *et al* (1934), Fig 4	Healthy subject
16	von Deesten *et al* (1934), Fig 5	Healthy subject
17	Wood *et al* (1935), Fig 1	Healthy subject
18	Wilson *et al* (1944), Fig 11	Ulcerative colitis
19	Wolferth *et al* (1947), Fig 1	Healthy subject
20	Goldberger (1947), Fig 62	Healthy subject
21	Own case	Hypertension
22	Own case	Aortic stenosis
23	Own case	Hypertension, cerebral hæmorrhage, uræmia
24	Own case	Stokes Adams syndrome and partial block
25	Own case	Aortic stenosis
26	Own case	Hypertensive heart failure
27	Stenström (1927), Fig 24	Heart failure
28	Wood *et al* (1935), Fig 2	Ventricular septal defect
29	Evans *et al* (1937), Fig 4	Congenital heart disease
30	Evans *et al* (1937), Fig 5	Mitral stenosis, fibrillation, hypertension
31	Evans *et al* (1937), Fig 7	Fibrillation
32	Evans *et al* (1937), Fig 8	Hypertensive heart failure
33	Evans *et al* (1937), Fig 9B	*Heart failure*
34	Evans *et al* (1937), Fig 10	Hypertension
35	Evans *et al* (1937), Fig 12	Aortic stenosis
36	Evans *et al* (1937), Fig 15A	Heart failure
37	Yater (1938), Fig 1	Mitral disease
38	Conneau *et al* (1938), Fig 1	Rheumatic fever
39	Katz (1941), Fig 389	Hypertension
40	Wolferth *et al* (1947), Fig 2	Angina of effort
41	Wolferth *et al* (1947), Fig 3	Stokes Adams syndrome
42	Own case	Recent cardiac infarction
43	Own case	Cardiac infarction 2 years ago
44	Own case	Cardiac infarction 2 months ago
45	Own case	Cardiac infarction 8 years ago
46	Own case	Cardiac infarction 5 years ago
47	Levine (1929), Fig 58	Recent cardiac infarction
48	Appelbaum *et al* (1934), Fig 28	Cardiac infarction
49	Master *et al* (1938), Fig 2	Recent cardiac infarction
50	Master *et al* (1938), Fig 7A	Recent cardiac infarction
51	Master *et al* (1938), Fig 8	Recent cardiac infarction.
52	Katz (1941), Fig 386C	Recent cardiac infarction.
53	Wilson *et al* (1944), Fig 29	Recent cardiac infarction
54	Wilson *et al* (1944), Fig 37	Recent cardiac infarction
55	Wilson *et al* (1944), Fig 38	Recent cardiac infarction
56	Goldberger (1947), Fig 79A	Recent cardiac infarction
57	Carlotti (1947), Fig 8A	Recent cardiac infarction
58	Curtis Bain *et al* (1947), Fig 17A	Recent cardiac infarction
59	Curtis Bain *et al* (1947), Fig 17B	Recent cardiac infarction.
60	Soulié *et al* (1948), Fig 7	Cardiac infarction 9 months ago
61	Own case	Cardiac infarction some months ago
62	Own case	Cardiac infarction some months ago
63	Own case	Cardiac infarction 3 weeks ago
64	Own case	Recent cardiac infarction
65	Levine (1929), Fig 9	Recent cardiac infarction
66	Levine (1929), Fig 58	Old cardiac infarction
67	Evans *et al* (1937), Fig 11	Old cardiac infarction
68	Master *et al* (1938), Fig 1	Recent cardiac infarction
69	Master *et al* (1944), Fig 1B	Recent cardiac infarction
70	Wilson *et al* (1944), Fig 39	Old cardiac infarction
71	Wolferth *et al* (1947), Fig 4	Recent cardiac infarction
72	Carlotti (1947), Fig 8B	
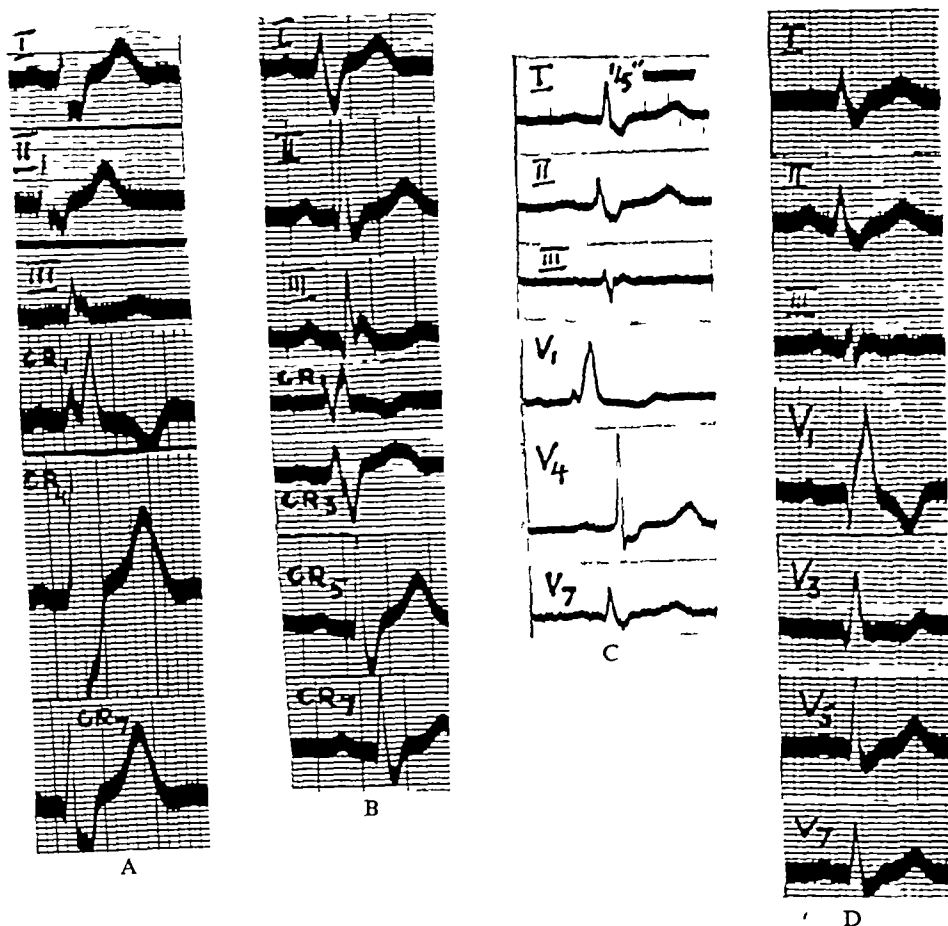
Fig 1 —Right bundle branch block in healthy subjects   (A) Case 3   (B) Case 7   (C) Case 1
(D) Case 8

isoelectric line up to the beginning of the T wave, or it started slightly below this line to merge almost immediately into the descending limb of the T wave, the T wave was inverted in all cases except one (Fig 1C)   In left præcordial leads small Q deflections were frequent, an S wave was shown in all records and T was upright   As right branch block caused T inversion in right præcordial leads, so it tended to increase the voltage of T in left præcordial leads

RIGHT BUNDLE BRANCH BLOCK WITH HEART DISEASE OTHER THAN CARDIAC INFARCTION

This group consisted of 21 cases (see Table, Cases 21–41)   In the limb leads   Q I and Q II appeared with the same frequency as in the previous group, the upstroke of R and the beginning of the downstroke of S had generally the same characteristics as those described for healthy subjects, but

there were 2 cases in this group with a QRS complex of low voltage   In left ventricular hypertrophy from hypertension or aortic valvular disease (Fig 2 and 3), the R-T segment often showed depression and a downward slant in lead I, or I and II, the T waves were upright in leads I and II in all cases, though occasionally of low amplitude   Left ventricular preponderance never caused T inversion in right bundle branch block, T inversion shown in normal intraventricular conduction in lead I from left ventricular preponderance was abolished with the onset of right branch block (Fig 2, B and C), and the amplitude of T waves low in normal conduction was increased in block   Chest leads were taken in 11 cases of this group, and included right præcordial leads in 7   In lead CR1 or V1, a small Q deflection was recorded once (Fig 2A), the QRS complex showed the bifid R already described, and the T wave remained inverted   In records from patients

A

B

C
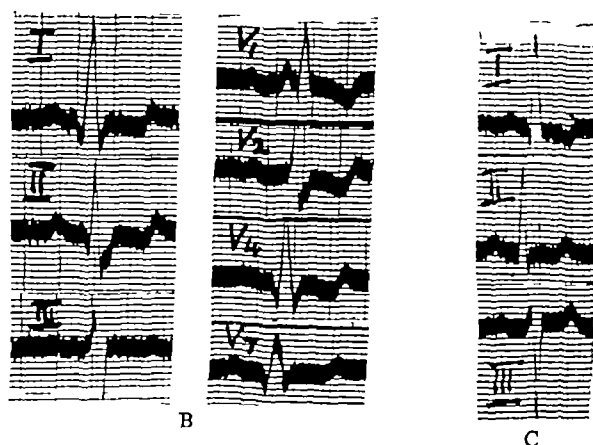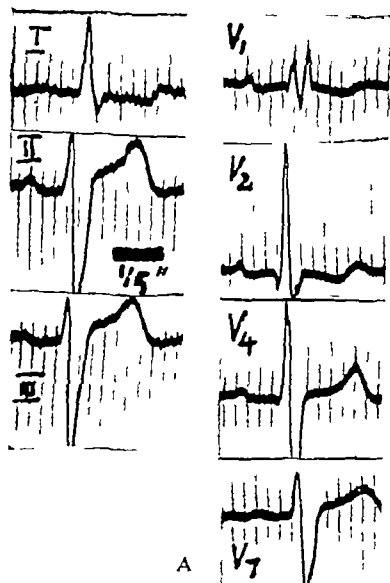
FIG 2 —Right bundle branch block and left ventricular pre ponderance in patients with aortic stenosis (A) Case 21 (B) Case 24 (C) Case 24 in normal intraventricular conduc tion

A

B

FIG 3 —Right bundle branch block and left ventricular preponderance in patients with severe hypertension (A) Case 23 (B) Case 26

with left ventricular hypertrophy, right præcordial leads showed the same type of slanting R–T segment as did lead I, and the T wave was upright in some cases (Fig 2A and 3B) In apical leads and in leads from the left lateral chest wall, Q deflections were seen in 4 cases, and the deep S of right branch block was present in every tracing In records with left ventricular preponderance, the R–T segment returned to the isoelectric line, or was even raised above it, as the leads were moved to the left of the chest (Fig 2 and 3) The T wave remained upright in all left præcordial positions even as far left as V7 None of the patients with left ventricular preponderance were under digitalis treatment

RIGHT BUNDLE BRANCH BLOCK IN CARDIAC INFARCTION

Nineteen cases of anterior infarction were collected (see Table, Cases 42–60) In the limb leads Q deflections in leads I and II were neither more frequent nor more conspicuous than in the previous two groups A low voltage QRS complex was seen eight times, similar low voltage deflections were also recorded with heart disease other than infarc tion, four cardiograms showed a QRS complex of low voltage and w-shape The R–T segment in lead I was of coronary type showing elevation and bowing, in 3 patients, in 8 other cases the R–T segment was elevated in lead I or II, but without bowing, and it was often followed by an upright T wave of normal appearance (Fig 4, A and B), this

FIG 4 —Right bundle branch block and anterior cardiac infarction (A) Case 42 (on day of infarction) (B) Case 42 (7 days later) (C) Case 43 (D) Case 44 (E) Case 46
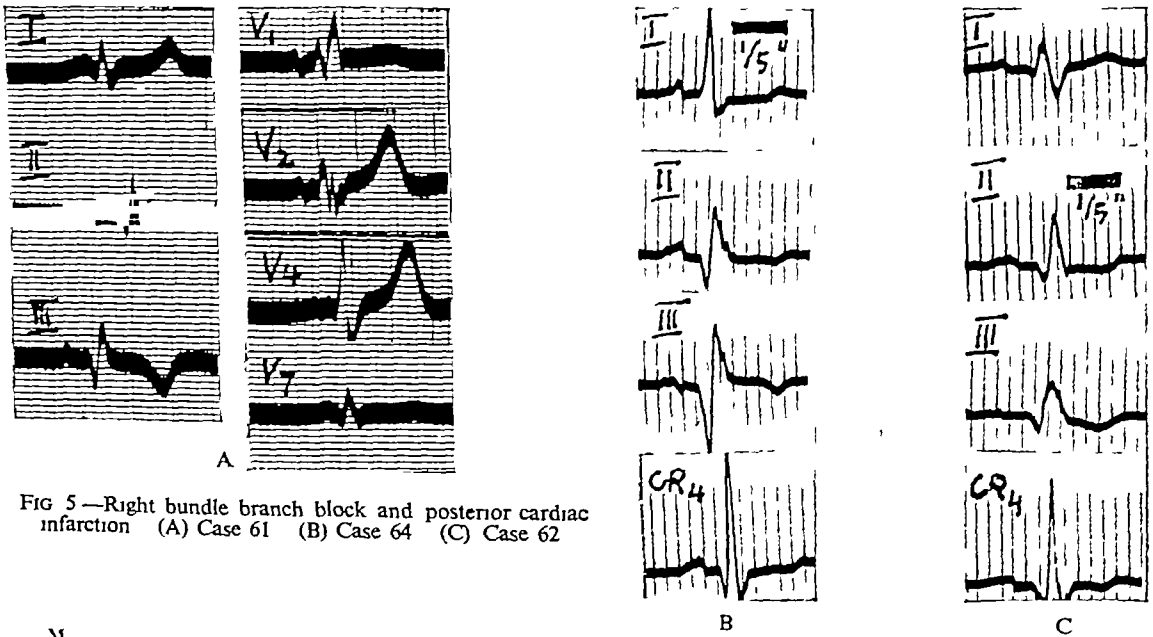
FIG 5 —Right bundle branch block and posterior cardiac infarction (A) Case 61 (B) Case 64 (C) Case 62

form was presumably due to the tendency of the T wave to remain upright in right branch block, and so to prevent the development of typical "coronary" changes   In contrast to the previous two groups, T inversion was a frequent finding in the later stages of infarction, it occurred in lead I in 7 and in lead II in 5 out of 19 cases (Fig 4, C and D) A number of extrasystoles were seen and examined, but they showed no modifications indicating infarction

Chest leads were taken in 17 of the 19 cases, and included right præcordial leads in 11   Lead CR1 or V1 indicated the lesion in 9 out of 11 cases in which this lead was taken, by showing a Q deflection followed by a late R with a single peak, recent cases also showed coronary R–T changes   Involvement of this lead seemed to occur more often in right branch block than in normal conduction and to be characteristic of the block, it was not due to a greater frequency of septal infarcts in records with bundle branch block as there was one patient (Case 54) whose cardiogram after infarction showed a characteristic Q 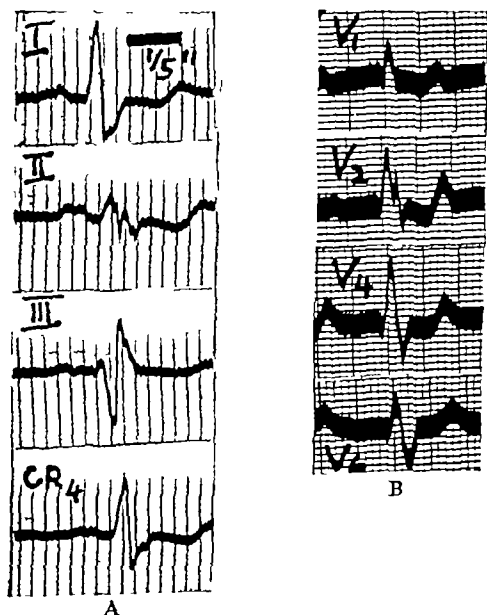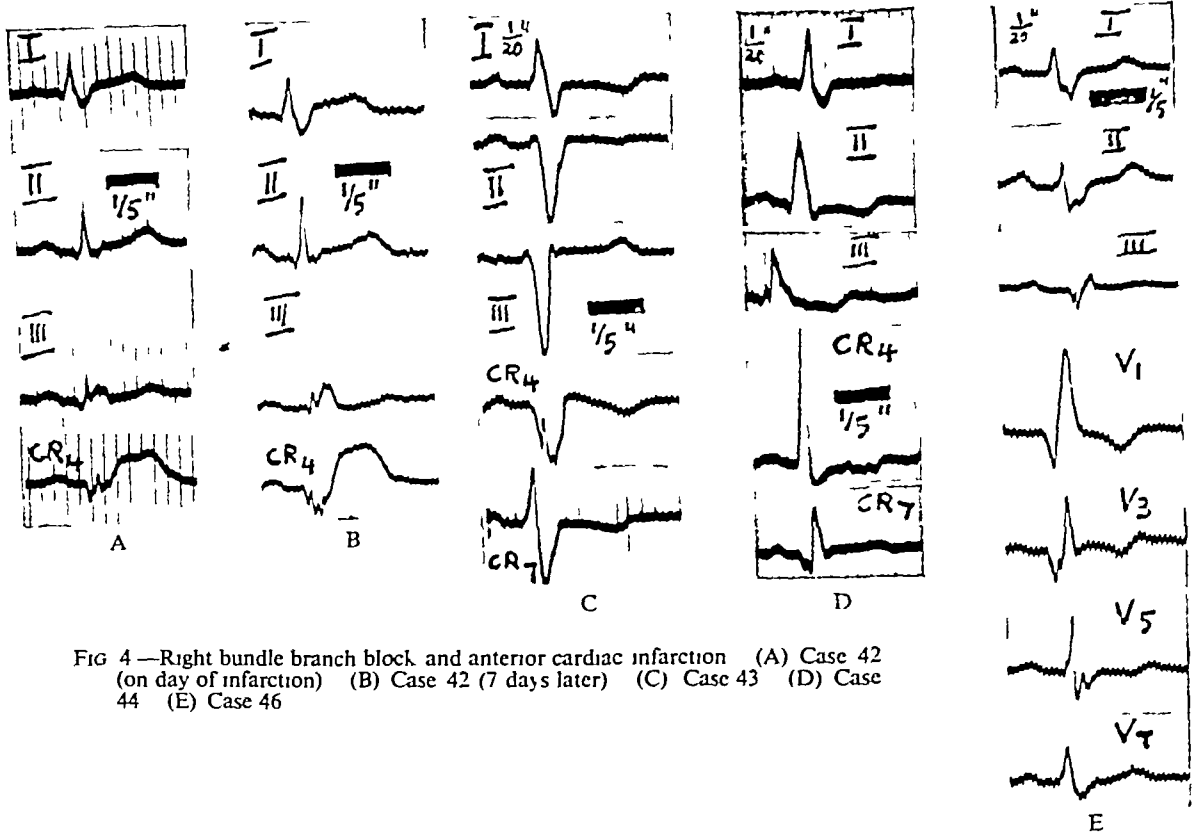in lead V1, only in block and not at other times, in normal conduction   The Q deflection or R–T changes of infarction extended to the apical lead in 5 patients, but were confined to right præcordial leads in 3 (Fig 4E), in such cases it was important to be certain of the absence of a small initial R wave (compare Fig 1D and 4E) Lead V1 remained unaffected in two records   in one the lesion was shown in the apical lead (Case 60), and in the other in a lead from the left lateral chest wall (Case 57)   Six præcordial cardiograms did not include lead CR1 or V1, in five, changes of infarction appeared in the apical lead (Fig 4, A to C), and in one in lead CR7 (Fig 4D)

There were 12 cardiograms in this series showing posterior wall infarction (see Table, Cases 61–72) With the exception of one case of old infarction (Case 71), all tracings exhibited large and significant Q deflections in lead II (Fig 5), Q I was no more frequent than in any previous group, Q III and inversion of T III, though present in most records, were not significant as they also occurred in right branch block without infarction   T I was upright in all cases, but T II was often abnormal   A coronary type of R–T segment in lead II or III or both was seen in 4 cases   The chest leads analysed in this group included 9 records with apical leads, and 4 with more complete cardiograms   In 3 out of 4 cases, T was upright in lead CR1 or V1 (Fig 5A), apical leads showed Q deflections in 4 cases and R–T depression in recent posterior infarctions

DISCUSSION

The preceding analysis has demonstrated a number of modifications of the electrocardiogram of cardiac infarction caused by the simultaneous presence of right bundle branch block   Soon after the common form of right branch block was first recognized in America by Wilson et al (1934) and in England by Evans and Turnbull (1937), the combination of right branch block and infarction was examined by several authors, and especially by Wilson and his collaborators   For the limb leads, Rosenbaum et al (1944) reported the absence of significant Q deflections in lead I in dogs with experimental right branch block and anterior infarction   This observation was confirmed for the human cardiogram in this study   The even R–T elevation, without bowing and with an upright T following it, described here for leads I and II in anterior infarction with right branch block, was not previously discussed, although it was a frequent finding in various published tracings, it was also well shown in cardiograms of dog experiments (Rosenbaum et al (1944), dogs 66 and 71, and Unghváry (1942))   Inversion of T in lead I and II is, of course, a classical sign of anterior infarction, and its significance in records with right branch block had previously been reported by Master, Dack, and Jaffe (1938)   The modification of the T wave pattern noted in this study concerned the tendency of of T to remain upright in all cases of right branch block, and especially also in cases with associated left ventricular preponderance   T wave changes, therefore, occurred at a later stage of infarction than in normal conduction, and the significance of T inversion, when present, was enhanced

Wilson et al (1944) first described the characteristic præcordial cardiogram of anterior infarction, with a Q replacing the initial R of right branch block in lead V1, in the present series, right branch block caused no important modifications of the signs of infarction in apical leads or in leads from the left lateral chest wall, but lead CR1 or V1 indicated the infarct more often than would be expected in normal intraventricular conduction, this seemed independent of the septal extension of the infarcted area expected in many cases of branch block

No modifications of the limb lead or præcordial cardiogram of posterior infarction have previously been reported   A number of cases here discussed showed upright T waves in chest lead CR1 or V1

It is now possible to describe, with the help of the preceding analysis, the electrocardiographic signs diagnostic of infarction in the presence of right bundle branch block   The following signs were significant in the limb leads   a w-shaped QRS complex of low voltage and a coronary R–T segment with a coronary T wave in lead I, an even elevation of the R–T segment followed by a normal T wave

and, later, inversion of T in lead I or II or both The w-shaped QRS complex could not be accepted as conclusive because of the difficulty of distinguishing, in a given case, this form and any other low voltage QRS complex without the w-shape Inversion of T in lead II was significant except in cases showing the classical and rare form of right branch block it was, therefore, of no value if R in lead III was conspicuous and taller than R in lead II, and if R in lead I also was of low voltage Using these signs, the lesion was diagnosed in the limb leads in 16 out of 19 cases of anterior infarction

This result is not in agreement with previous observations Wood, Jeffers, and Wolferth (1935) first reported that right branch block may mask the signs of infarction in the limb leads Master Dack, and Jaffe (1938) stated that in the presence of right branch block infarction could be diagnosed in two thirds of the cases, and that præcordial leads were more helpful than limb leads Stokes (1947) quoted this opinion and agreed with it Wilson *et al* (1944) reported that in right branch block signs of infarction were rare in the limb leads, but were usually shown in præcordial tracings, this view was also expressed by Goldberger (1947) and Carlotti (1947), Rosenbaum *et al* (1944) came to the same conclusion for dogs with experimental right branch block and anterior infarction The explanation for this difference of opinion came from a consideration of the criteria of infarction in the limb leads In the past, limb lead cardiograms have not been regarded as diagnostic of infarction if the classical signs of infarction were absent It was here shown that the diagnosis can often be made if the signs include R–T elevation or T inversion, and if the tracings are not expected to show significant Q deflections

Diagnostic signs of infarction with conspicuous Q deflections and classical R–T changes were seen in the præcordial cardiogram of all 19 cases here reported, in tracings with signs of infarction in apical or left lateral chest leads, the limb leads showed the lesion as well, but right præcordial leads indicated infarction in 3 records in which all other limb and chest leads were negative, in such cases it was important to be certain of the absence of a small initial R wave in lead CR1 or V1

The diagnosis of posterior infarction could be made from the presence of conspicuous Q deflections in lead II and from coronary R–T changes in lead II and III in all but one case reported here, the præcordial cardiogram showed upright T waves in lead CR1 or V1 in some tracings, this sign had no diagnostic significance as it was not seen in all records of posterior infarction and because it was also present in other conditions, especially in left ventricular preponderance, yet it gave valuable help in the analysis of some tracings In Case 71 an upright T wave in lead CR1 was the only abnormality in limb and chest leads of a patient known to have had posterior infarction in the past, and a flat T wave in a case of anterior infarction (Case 56) suggested an associated lesion, which was shown to be an old posterior infarct by the limb leads, an upright T in lead V1 of another patient with anterior infarction (Case 60) was explained when left ventricular hypertrophy was found on necropsy

For the purposes of clinical diagnosis, the limb leads furnished all essential information for the diagnosis of cardiac infarction in most cases, they also indicated left ventricular preponderance Chest leads CR1 or V1 confirmed the presence of right branch block and disclosed a small number of infarcts not shown by any other lead The combination of limb leads with lead CR1 or V1 revealed all lesions recorded with more numerous chest leads and thus satisfied the clinical needs in the 31 cases of right bundle branch block and cardiac infarction reviewed here

SUMMARY AND CONCLUSION

It was the object of this paper to inquire into the modifications of the electrocardiogram of cardiac infarction in the presence of right bundle branch block, and to examine the criteria necessary for the diagnosis of infarction The investigation consisted in an analysis of cardiograms with right branch block taken from healthy subjects, from cases with heart disease other than infarction, and from patients with cardiac infarction Twenty-three patients with right branch block came under personal observation and 49 reported cases were added Right bundle branch block is shown to cause certain modifications of the cardiographic signs of infarction In the limb leads of anterior infarction, significant Q deflections are absent in lead I, the R–T segment often assumes a characteristic shape in lead I or II, showing elevation without bowing, and is then followed by a T wave of normal appearance, when T inversion takes place in lead I or II, it more certainly indicates infarction than T inversion in normal conduction, because this change does not occur from left ventricular preponderance in right branch block In the præcordial cardiogram the infarct is more often shown in CR1 or V1 leads than would be expected in normal conduction, involvement of this lead appears to be independent of the septal extension of the infarct expected in cases of bundle branch block Right branch block does not change the classical signs of posterior infarction in the limb

leads, in chest leads, the T wave is upright in lead CR1 or V1 in some cases of posterior infarction

The diagnosis of anterior infarction can be made in the limb leads in many cases if the signs include R–T elevation or T inversion, and if the tracings are not expected to show significant Q deflections, infarction is shown by apical or left lateral chest leads when it is also shown by the limb leads, but lead CR1 or V1 occasionally registers the lesion when all other leads are negative   The diagnosis of posterior infarction is made from the presence of conspicuous Q deflections in lead II and of coronary R–T changes in lead II and III   The præcordial cardiogram may show upright T waves in lead CR1 or V1, although this sign has no diagnostic value, it is helpful in the interpretation of some electrocardiograms

The limb lead cardiogram in conjunction with lead CR1 or V1 provides the necessary information for the diagnosis of cardiac infarction and right bundle branch block

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RIGHT VENTRICULAR STENOSIS
(BERNHEIM S SYNDROME)

BY

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Since this clinical state was first described by Bernheim in 1910, very little has appeared in the English language or in journals easily accessible in this country, or at all in recent years   The recent paper on the subject by Russell and Zohman (1945) gives references many of which we cannot check   A good deal was written in 1930 and 1931, and there were seven papers associated with the name of Mazzei and five with that of Martini   We record these cases to draw attention to a pathological state that appears to explain satisfactorily certain rather curious clinical phenomena

The essential feature of the syndrome is what appears to be a clinical paradox   There are conspicuous features of apparent failure of the right side of the heart in a patient with a lesion affecting the left side   The explanation for this was offered by Bernheim (1910), who pointed out that the septum of the ventricles bulged into the cavity of the right ventricle, and so prevented it filling   Podesta (1936) has called it dextroventricular stenosis   The progress of the disorder has been divided into two stages by Mazzei (1931)   In the first the infundibulum becomes dilated and so allows the flow of blood to be maintained despite the interference with the filling of the ventricle   We have satisfied ourselves by means of casts taken of the cavity of the upper part of the right ventricle in two cases that this is so   In the second phase this adjustment becomes inadequate and the signs of hepatic and jugular engorgement are seen   The pulmonary circulation remains unaffected until near the end, when a final congestion of the lungs may appear

CASE REPORTS

The clinical and post-mortem findings of our five cases now follow and will be discussed and compared with others reported

Case 1   A labourer, aged 32, was admitted to

hospital in January 1945 complaining of swelling of the legs and feet and of fatigue, but had no shortness of breath   As a child he had attended hospital on account of his heart, and had not been allowed to play games at school   Since leaving school, however, he had been well and had lived an unrestricted life

The patient was a fat, well-built man   There was no cyanosis   The veins in the neck were not obviously engorged, but the liver was enlarged about one and a half inches below the edge of the ribs   The backs of the legs and the buttocks were swollen   His aspect generally was somewhat pale

The cardiac dullness extended three-quarters of an inch to the right of the sternum   The apex beat was forcible and situated five and a half inches to the left of the midline in the sixth left interspace   A very loud harsh systolic murmur was best heard three inches from the midline in the fifth left interspace   This murmur was accompanied by a thrill   The murmur was conducted to the mitral and pulmonary areas and to the left axilla, but not particularly upwards   The heart sounds at the apex were quite loud, while those at the base were faint, the pulmonary second sound was louder than the aortic   The pulse was regular, of poor volume, and not anacrotic, with a blood pressure of 100/80   Screening of the heart showed that the right auricle was obviously engorged, the left ventricle was not conspicuously enlarged, and the pulmonary vessels were somewhat prominent   The aorta was normal (Fig 1)

Barium in the œsophagus showed slight engorgement of the left auricle   The cardiogram showed no axis deviation, the rhythm was normal but the effect of digitalis was apparent in R–T negativity in all three leads (Fig 2)   The diagnosis appeared to have lain between pulmonary stenosis, aortic stenosis, and patent interventricular septum   The site of the murmur, the predominance of right ventricular failure, the absence of an anacrotic pulse

145

FIG 1 —Case 1   Some engorgement of pulmonary veins but lungs translucent
Right auricle full   left ventricle enlarged

and the freedom from dyspnœa, also the equivocal cardiogram, made one decide upon the last, particularly in view of the presence of the lesion in childhood

At first, treatment for the congestive heart failure was successful   Mercurial diuretics were given freely and he was able to go to a convalescent home After a month or two he returned with further development of failure   In spite of treatment the anasarca gradually returned and steadily increased He was never orthopnœic and could lie fairly flat in bed   A pulmonary infarct occurred, and he slowly deteriorated and died

Autopsy   There was gross anasarca, profuse ascites, and a moderate hydrothorax on both sides There was no pulmonary œdema and the lungs were not grossly engorged   their dryness was remarked

on at the time   The heart was very large—720 g The left ventricle showed gross hypertrophy, the septum being very thick and bulging extensively into the right ventricle   This was considerably dilated, particularly in the infundibulum   The aortic valves were stenosed as a result of congenital fusion and subsequent calcification   The appearance was that of a bicuspid valve   Calcification was extensive, and in the depths of the anterior cusp there seemed to be traces of a small raphe The interventricular septum was not patent   The coronary sinus was greatly dilated, perhaps by the high pressure in the right auricle   There was gross passive engorgement of the liver

Comments   The diagnosis was missed in this case because of the site of the murmur and the absence of confirmatory signs of aortic stenosis

The freedom from embarrassment of the pulmonary circulation, the absence of left axis deviation in the electrocardiogram, and the conspicuous predominance from the first of the results of right side failure made the diagnosis in favour of a patent interventricular septum (Maladie de Roger) for pulmonary stenosis did not appear to be in any way indicated

Reflection on the findings at autopsy suggested that the clinical manifestations indicated Bernheim's syndrome The stenosis of the aortic valves should have sooner or later led to failure of the left ventricle, but right ventricular failure was predominant from the first On Bernheim's theory the encroachment on the cavity of the right ventricle would have been responsible for the early state of the failure of the right side The absence of engorgement and oedema of the lungs post-mortem was very striking The absence of left axis deviation agrees with some cases regarded as examples of Bernheim's syndrome, but it seems likely that unipolar limb leads would have shown that the heart was vertical, and consequently the axis deviation due to left ventricular hypertrophy was lacking

The incorrect diagnosis shows how hard it may be to interpret obvious physical signs, and on reflection it is difficult to see what might have led one to suppose that aortic stenosis was really the cause of the murmur and thrill Failure of the right ventricle would have been expected to develop early had the ventricular septum been patent

Case 2 A woman aged 62, became more and more out of breath on exertion This symptom was first noted on hills and long walks, and later on climbing stairs For the last six months she had been breathless on any slight activity During the winter before coming into hospital she had been confined to bed for two months, there had been several attacks of bronchitis She was now rather breathless at rest There was slight swelling of the ankles, but the liver and the external jugular veins were not engorged The heart rate was 100, with the rhythm regular The pulse showed alternation and the wave was slightly anacrotic The blood pressure was 220–210/145 There was thickening of the brachial and retinal arteries The apex beat was weak and diffuse, extending five inches to the left of the midline, in the fifth intercostal space In the mitral area a presystolic gallop rhythm was audible

FIG 2   FIG 3   FIG 4

FIG 2 —Case 1   Standard three leads, showing bigeminy and negative T waves, but no left axis deviation
FIG 3 —Case 2   Standard three leads, showing left axis deviation
FIG 4 —Case 4   Standard three leads, showing left axis deviation

At the base, in the aortic area a rough systolic murmur could be heard, extending into the arteries of the neck No thrill was palpable The aortic second sound was faint, at the bases of the lungs were fine scattered crepitations, the skiagram showed that the pulmonary veins were engorged The cardiogram (Fig 3) showed evidence of left ventricular hypertrophy The diagnosis was failure of the left ventricle due to hypertension and slight aortic stenosis Failure of the right ventricle was

to 22 from 30 a minute On the evening of the third day she died suddenly

Autopsy There was gross œdema and venous congestion The liver was "nutmeg," weighing 1615 g The spleen showed severe chronic conges tion The heart weighed 600 g The left ventricle was enormously hypertrophied, the wall being about 30 mm thick (Fig 5) The septum, which was 20 mm thick, bulged into the cavity of the right ventricle The aortic valve was stenosed, the cusps
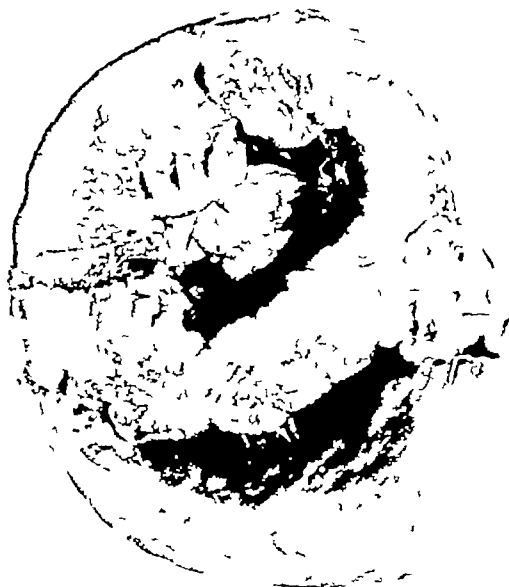
FIG 5 —Case 2 Transverse section of ventricles looking towards the base The thickened septum bulges into the right ventricle

developing Under treatment she improved and kept fairly well on leaving hospital until six months later, when there was a further attack of bronchitis This time there was rapid development of œdema and venous congestion The liver was three inches below the ribs, and there was anasarca to the waist The jugular veins were prominent half way up the neck She was rather blue, but not orthopnœic, and could lie fairly flat A few crepitations were heard in the lungs, the pulmonary second sound was loud After three days in hospital the respiratory rate fell

being fused and calcified A slight ridge below the free margin suggested a rheumatic infection in the past The lungs, in contrast to the liver, were free from engorgement, and showed hardly any œdema, the right weighed 550 g (normal 500 g), and the left 380 g (normal 420 g) Microscopical section showed some engorgement and scattered heart failure cells only There was but a trace of fluid in the left pleural sac There was nothing to explain the sudden death except the aortic stenosis

Comments This patient, developed gradual

failure of the left ventricle about two years before her death Œdema of the ankles did not appear until the last six months The final failure appears to have been precipitated by an attack of bronchitis and was marked by severe venous congestion which increased rapidly in the last three weeks Although she was breathless on admission to hospital, this was soon relieved The important point is the freedom of the lungs from œdema and engorgement post-mortem It would appear likely that the bulging of the septum into the right ventricle prevented the lungs from being overfilled although the aortic stenosis and hypertension affecting the left ventricle would have made this a likely finding It is true that it is common to find failure of the right ventricle following that of the left in such cases as these and this has always been regarded as a true back pressure " phenomenon In this instance it would seem more probable that the cause was different, otherwise the lung would have shown the usual intense engorgement associated with a failing left ventricle The course of the illness suggests that in the earlier phases the lungs may have been involved but that the development of the stenosis of the right ventricle relieved them

Case 3 A woman, aged 63, had complained of dyspnœa, gradually increasing in intensity, for the previous four years During the last six months she had had acute attacks of breathlessness at night and had often been orthopnœic In the last month the legs had become œdematous, and since then she had been confined to bed Auricular fibrillation was present, with a heart rate of 70, for she had been taking Guy's pill twice a day for two years The heart was greatly enlarged to the left, with a heaving apex beat A rough systolic murmur was heard at the apex The pulmonary second sound was abnormally loud Crepitations were heard at the bases of both lungs Œdema was present halfway up the thighs, and there was a small sacral pad Ascites was present, and the liver was enlarged two inches below the ribs The cervical veins were engorged

A cardiogram showed auricular fibrillation The limb leads indicated right axis deviation, but the præcordial leads confirmed the clinical evidence of left ventricular hypertrophy

It was supposed that she had previously had high blood pressure and was now in the later stages of congestive failure with auricular fibrillation She refused to come into hospital and deteriorated steadily at home, but after a month she had to be admitted There was now massive œdema of the legs and abdominal wall, and even the hands were somewhat swollen There were no signs in the

lungs and the breathing was easy she was able to lie quite flat without discomfort

The cardiogram now showed advanced right axis deviation with a vertical heart but the chest leads still indicated hypertrophy of the left ventricle
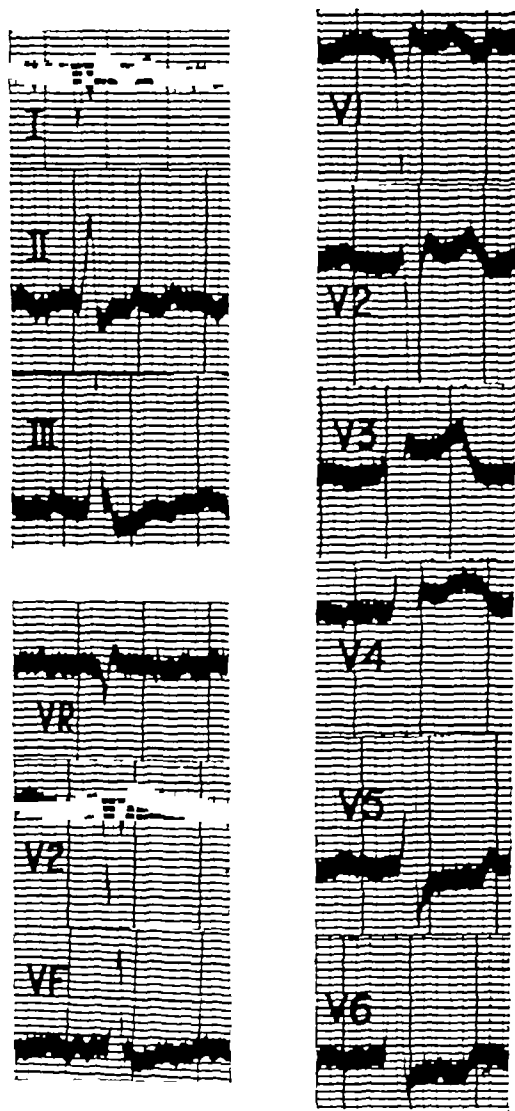
Fig 6 —Case 3 Standard leads show right axis deviation Unipolar limb leads show a vertical heart Unipolar chest leads show hypertrophy of the left ventricle

(Fig 6) She slowly got worse, and she died a month later

The clinical diagnosis of Bernheim's syndrome was suggested on the finding of gross congestive failure in a case of predominantly left-sided disease

together with freedom from embarrassment of the pulmonary circulation   The findings at autopsy confirmed this diagnosis

Autopsy   Œdema was present in the lower parts of the body   There was no free fluid present in the pleural sacs, the lungs were well ærated throughout and free from œdema   Venous congestion was not conspicuous   The weight of the right lung was 420 g (normal 500 g), and of the left lung 390 g (normal 425 g)

Section of the lungs showed no evidence of chronic venous congestion   On the whole congestive changes were mild   An early bronchopneumonia was developing in the right lower lobe, and here there appeared œdema in the alveoli and congestion of capillaries

myocardium showed a generalized increase in fibrous tissue which was evenly scattered between the muscle fibres   These fibres themselves showed no degeneration but were definitely hypertrophied The liver was enlarged (1480 g) and showed evidence of venous congestion   The kidneys were slightly contracted and granular   There was much free fluid present in the abdomen

Comments   The conspicuous finding was hypertrophy of the myocardium of the left ventricle, with great increase in thickness of the interventricular septum, which encroached upon the cavity of the right ventricle   The conspicuous venous engorgement of the portal system was in striking contrast with the absence of engorgement in the pulmonary circulation

FIG 7 —Case 3   Transverse section of the ventricles looking towards the base   The thickened septum bulges into the right ventricle

The heart was greatly enlarged, weighing 810 g The most striking feature was the concentric hypertrophy of the muscle of the left ventricle   The wall of the right ventricle was also hypertrophied, and the thickness of the interventricular septum was much increased   The thickness of the right ventricle about halfway up was 4 to 5 mm, and that of the left ventricle about the same level was 20 mm The septum was 20 to 24 mm in thickness throughout   The cavity of the right ventricle was encroached upon by the bulge of the thickened interventricular septum into it (Fig 7)   There was no apparent dilatation of this chamber   The internal capacity was therefore very considerably diminished The right auricle was dilated   All valves were normal   There were also numerous areas of atheromatous degeneration in the coronary arteries   The

On these findings the clinical diagnosis of Bernheim's syndrome would appear to be confirmed

Case 4   A woman, aged 54, first came under observation in 1932 when she attended hospital for a mild toxic goitre   This was removed and she made a good recovery

In 1938, when she was 47, she again attended hospital   She had had several severe paroxysms of auricular fibrillation   There had been a swelling of the ankles and pain over the front of the chest   The signs in the heart now showed aortic stenosis

In 1945, when she was 54, she was again admitted to hospital   During the past seven years she had had attacks of fibrillation from time to time, and in the last year or two she had had a good deal of pain under the sternum on walking   Breathlessness had

not been a conspicuous symptom, there never had been any orthopnœa There was a good deal of swelling of the ankles and a considerable pad in the sacral area The veins in the neck were considerably engorged and filled from below up to about four inches above the level of the right auricle when she was sitting nearly upright The liver was a good deal enlarged The apex beat reached the sixth space five inches from the midline There was a typical murmur of aortic stenosis The aortic second sound was not audible Auricular fibrillation came and went There was, however, no satisfactory improvement in the signs of congestive heart failure digitalis and diuretics were ineffective gradually the œdema became more general and her condition deteriorated She was never in any way breathless and she gradually sank and died The electrocardiogram had shown auricular fibrillation, with left axis deviation

It was noticeable that this patient, who had evidently had aortic stenosis for a good many years never complained of shortness of breath The final phase of heart failure lasted two months and was marked by symptoms of failure of the right ventricle, whereas one would have expected a phase of left ventricular failure

Autopsy There was generalized anasarca, a few ounces of fluid were present in each pleural sac but the lungs were remarkably dry, but little engorged and quite free from œdema The right weighed 510 g (normal 500 g) and the left 390 g (normal 425 g) The heart weighed 540 g There was much engorgement of the right auricle and of the great veins The right ventricle was full, the left ventricle was greatly hypertrophied, and the septum was very thick and bulged prominently into the cavity of the right ventricle The tricuspid ring was slightly enlarged The aortic valves were fused, so that a small slit-like opening only was left The valves were heavily calcified and a ridge of nodular calcium deposit seemed to mark a raphe where the commissure of the two anterior cusps might have been These were probably congenital bicuspid aortic valves which had become calcified The stenosis had presumably developed progressively in the course of the last fourteen years

Comments In this case it is notable that the pulmonary circulation escaped engorgement right up to the end One might conclude that this was an example of Bernheim's syndrome in which a terminal ' failure " of the right side of the heart occurred, without any indications of failure of the left ventricle The presence of aortic stenosis would have led one to expect symptoms of left ventricular failure, but in this case again it would appear that engorgement upon the cavity of the right ventricle

by the bulging septum precipitated the failure of the right side and protected the lungs

Case 5 A clerk, aged 58, a tall, thin man, was sent to hospital with severe epistaxis He was found to have a blood pressure of 220/130, some enlargement of the left ventricle, the apex beat being of a powerful, thrusting character in the sixth intercostal space, four and a half inches from the midline The peripheral arteries were thick, and the ischæmic, narrow retinal arterioles compressed the veins There was a trace of albumin in the urine There was no hepatic or jugular engorgement

A month later he returned with œdema halfway up the shins, and distended jugular veins whose fullness increased on compression of the abdomen The heart rate was 80 the beat regular A gallop rhythm was audible and with this was associated a duplication of the apex beat, which was easily seen and felt The aortic second sound was loud, but the pulmonary second sound was not The cardiogram showed left axis deviation with a negative T I (Fig 4) He had complained of no dyspnœa at all

In connection with the last of these indications of embarrassment of the pulmonary circulation it was noted that there were no crepitations at the bases of the lungs, the skiagram (Fig 8) showed no gross pulmonary engorgement

After three weeks' treatment all signs of failure had cleared up and the gallop rhythm had disappeared A few months later he died suddenly at home

Comment In this patient signs of congestive failure appeared in the systemic circulation, without the symptoms and pulmonary signs indicating prior failure of the left ventricle The skiagram was clear, the circulation time (decholin) of only 28 seconds was but little prolonged

For these reasons it seems correct to class this as an early case of Bernheim's syndrome Although there was ready response to treatment at first, death occurred a few months later

TYPES OF LESION

The underlying lesion in all these cases was either hypertension or aortic stenosis These cause concentric hypertrophy of the left ventricle Perusal of Bernheim's original series suggests that most of his patients were hypertensive, but no readings of the blood pressures were made The same causes were present in Russell's series and those of Mazzei (1931), also in the series of 9 reported by Casaffourth and Superviola (1936) Aortic stenosis was present in Olmer's patient (1933) and in that described by Glushien and Geer (1943) For some reason the

FIG 8 —Case 5   No indication of pulmonary engorgement   Hypertrophy of left ventricle

gross dilatation of the left ventricle caused by free aortic incompetence does not lead to right ventricular stenosis   Possibly the explanation is that the septum does not become sufficiently thick

Appearances in the skiagram   It has been claimed that distension of the right auricle is a feature (Glushein and Geer, 1943)   Two of our cases suggested this, but in Case 5, admittedly in an early stage (Fig 8), it is not present   The important point is the absence of engorgement of the fields of the lungs, although there may be slight overfilling of the pulmonary veins   We agree with other observers that the important triad is large left ventricle, clear lung fields, and full right auricle

POST-MORTEM FINDINGS

The encroachment of the septum upon the cavity of the right ventricle is very obvious when the ventricles are cut across at right angles to the long axis of the heart, midway between the apex and the base   This finding is likely to be missed when the ventricles are opened by V-shaped cuts, one down the outer border and the other upwards to the pulmonary artery (or aorta), as is usually done The transverse cut should really be made first of all in any post-mortem examination of the heart, this procedure might prevent the septal bulging from being overlooked, as we fancy it easily may be if the other procedure is followed

Photographs of the transversely divided ventricles are apt to be unsatisfactory, as by the time the heart has been opened the relative positions of the walls of the ventricles is lost and plugging with cotton wool and fixing in formalin easily spoils the true shape. We attempted to make a cast in two cases, of the upper part of the right ventricle and infundibulum. It is almost impossible to get a good photograph of this but we were satisfied that this part, the outflow tract, remains tubular in form, leading up to the pulmonary artery, thus giving an outlet relieving the constriction below as suggested by Russell and Zohman (1945) and earlier by Mazzei (1931)

THE LUNGS

The dryness of the lungs at autopsy, free from engorgement and œdema, as shown by their normal weight, is very striking. In all four cases this was a notable feature. This agrees, of course, with the relatively rapid circulation rate. Other observers have noted (e g Bernheim in five of his ten cases) infarcts in the lungs. whether these are due to emboli or thromboses is not clear

Cooke and White (1941) point out that in tricuspid stenosis there is conspicuous jugular engorgement with freedom from pulmonary congestion, so that the patient may be able to lie flat and even walk about with but little distress. Constriction of the pericardial sac presents the same apparent paradox, as Glushien and Geer (1943) have noted. The syndrome of Bernheim, by reason of the right ventricular stenosis, presents a third example of this curious combination of signs, it amounts, in fact, as Fishberg has stated (1940), to " a virtual tricuspid stenosis "

OTHER FINDINGS

The circulation rate In two of our patients (Cases 1 and 5) in which the observation was made the circulation rate was not grossly slowed, the arm to tongue time in both being 28 seconds. This is quite unlike the result one would expect in ordinary congestive failure, when it should be well over 40 seconds. Similar observations were made by Russell and Zohman (1945). As slowing chiefly occurs in the pulmonary circulation, the results indicate the relative freedom of the lungs from embarrassment

The cardiogram It will be noted that three of the curves in these cases of left ventricular hypertrophy show the expected left axis deviation in the three standard limb leads. In one this feature is absent and in another there is actually right axis

deviation. There has been a good deal of comment on this absence of the curve of left axis deviation, and it has been suggested that the bulging of the septum of the ventricles to the right may be the cause of these curves by affecting the electrical axis (Russell Zohman, 1945). It seems to us that the explanation is to be found in the unipolar limb leads which show that the heart is actually vertically placed in the chest and so the presence of the hypertrophy of the left ventricle cannot cause left axis deviation. This is not an uncommon finding in certain cases of left ventricular hypertrophy, quite apart from the presence of septal displacement to the right. We have recently noted three patients with aortic stenosis, two congenital in youths, and the third of the fibrocalcareous acquired type in an elderly man who showed no left axis deviation, but with unipolar limb leads showing the heart to be vertical

We therefore conclude that there are no cardiographic changes peculiar to Bernheim's syndrome

Further investigation It seems likely that two lines of investigation in such cases as these will be fruitful. It would be interesting to know what pressures may be revealed in the pulmonary artery by intracardiac catheterization. Angiocardiography should show the peculiar shape of the cavity of the right ventricle

TREATMENT

In these cases the question of venesection may arise. It would seem inadvisable to bleed in these circumstances, as a raised venous pressure is no doubt beneficial. Anything that reduces the venous pressure might do harm, and this perhaps applies to such drugs as digitalis and cardophylin

SUMMARY

Right ventricular stenosis (Bernheim s syndrome) may be found in patients with hypertension or aortic stenosis

The symptoms suggesting failure of the right ventricle come on early, and may be transient at first. The pulmonary circulation remains free from embarrassment, and the patient is free from orthopnœa, even to the end

The clinical diagnosis is confirmed at autopsy by the state of the lungs and transverse section of the ventricles

There are no cardiographic changes peculiar to the condition

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MITRAL STENOSIS IN LATER LIFE

BY

HAROLD COOKSON

Rheumatic heart disease with mitral stenosis has been regarded as a disease that produces symptoms in adolescence or early adult life, and death before the age of forty in the majority   It is admitted that occasionally the first symptoms will appear at the time of the menopause and that if the lesion is accompanied by hypertension, life may be prolonged beyond this period (Levine, 1945)   The few clinical observations that have been made on the subject, put the incidence of mitral stenosis beyond the age 50, at from 6 to 10 per cent (Coombs, 1924, Brenner, 1934, Hedley, 1940) (see Table I)   Levine and

TABLE I
MITRAL STENOSIS (OR RHEUMATIC HEART DISEASE)
(Proportion of cases over 50 years of age)

Clinical cases Author	Necropsy cases Author
1 Coombs (1924) 6%	1 Coombs (1924) 9%
2 Brenner (1934) 10%	2 Cabot (1926) 33%
3 Hedley (1940) 7%	3 Cookson (1930) 12%
	(M S and A F over age 48)
	4 Brenner (1934) 20%
	5 Hedley (1940) 11%
	6 White and Bland (1941)
	(5 cases, aged 73–85)
	7 Gelfman (1943) 33%
	8 Zeman (1945)
	(10 patients aged 60–74 with M S and subacute bacterial endocarditis)
	9 Karsner and Koletsky (1947)
	(48 with M S and aortic calcification in elderly patients)

Kauver (1941–42) were able to collect from the records of a hospital and a private practice over about a quarter of a century, 28 patients over 50 years of age with mitral stenosis and angina pectoris But more information is available from post-mortem studies than from clinical reports on the question

of mitral stenosis in the elderly   These reports give the percentage of patients dying with mitral stenosis at age 50 or more as from 9 to 33 per cent, figures that are so much higher than those for the clinical incidence as to suggest that the diagnosis is often missed during life (Coombs, 1924   Cabot, 1926, Cookson, 1930, Brenner, 1934, Hedley, 1940   White and Bland, 1941, Gelfman, 1943, Zeman, 1945   Karsner and Koletsky, 1947) (Table I)

The present investigation concerns 37 patients with mitral stenosis and one with mitral incompetence, ranging in age from 51 to 77 years   There were only 9 men, giving a sex ratio of more than 3 females to 1 male, which is higher than that for all cases of mitral stenosis   (Table II)   The

TABLE II
THIRTY-EIGHT PATIENTS WITH MITRAL DISEASE OVER FIFTY

Age	Number
51–60	26 (18 F 8 M)
61–70	8 (7 F 1 M)
71–77	4 (4 F 0 M)

predominance of women increased in each successive decade so that all patients over 70 were women   A greater number was seen in private than in hospital practice which is the reverse of the distribution for younger age groups   There was a clear history of rheumatic fever or chorea in 15, and in a further 8, a valve lesion or heart disease had been diagnosed in childhood or early adult life   In 5, the first known attack of rheumatic fever occurred at the age of 34 or later, and recurrent attacks after the age of 30 were mentioned in 2 others

All had lived actively and, though some admitted that they had never been capable of strenuous exertion because of shortness of breath, the general capacity for work was at least average   Of 23

155

women who were married, 18 had had children, in one case, five

INITIAL SYMPTOMS

When first seen, 32 of the 38 cases had established auricular fibrillation, 2 came under observation with paroxysmal tachycardia, 1 with paroxysmal fibrillation, and only 3 had normal rhythm In one of these last, fibrillation set in after a few weeks In 8 cases a sudden onset of symptoms, mainly palpitation and dyspnœa, was known to coincide with the occurrence of fibrillation or was strongly suggested by the history In 3, the first symptoms were due to cerebral embolism, in one to pulmonary infarction and in one to ischæmia of the legs Congestive failure was present in about one third of all cases when they were first seen, and this nearly always responded to appropriate treatment In a further third, systemic congestion developed during the period of observation and treatment which was generally a matter of years Failure under these conditions was resistant to treatment though some survived in a state of invalidism for months or years Systemic congestion with normal rhythm was observed in one patient only Two patients who died from the effects of left auricular thrombosis never showed signs of systemic congestion They had auricular fibrillation and symptoms for six months and four years respectively

DIAGNOSIS

The diagnosis of mitral stenosis in the patients in this series, was made on the presence of a rough, low-pitched diastolic murmur heard best at the apex beat or occasionally a short distance from it, as for example in the intercostal space above the apex The murmur begins very soon after the second sound, is decrescendo, dying away as a rule before the first sound, though rarely reaching it In this last event an impression of a crescendo presystolic murmur is possible even with auricular fibrillation The diastolic murmur may be so rough as to be unmistakably that of mitral stenosis, but more often it is softer, yet not of the blowing quality characteristic of the aortic diastolic murmur Nevertheless, when aortic incompetence was present, as it was in ten patients, mitral stenosis was not considered proved by a low pitched apical murmur, unless characteristic X-ray changes of mitral stenosis were present The diastolic murmur of mitral stenosis in the elderly requires careful and sometimes lengthy auscultation for its detection, and it may be quite inaudible in any but the long diastoles Mitral stenosis may of course exist when the only murmur is systolic There were two

cases of this type, in which the diagnosis was established post-mortem, but apart from these a mitral diastolic murmur had been heard in all, though not necessarily on every occasion the patient was examined Subsidiary signs of mitral stenosis were usually present, in order of frequency these were a sharp first sound, a third heart sound, accentuated pulmonary second sound, and flushed or cyanotic appearance of the malar eminence

HYPERTENSION

Levine (1945) remarked on the frequency of arterial hypertension in older patients with mitral stenosis, and indeed ascribed their longevity to this complication It is not easy, however, to determine the frequency of hypertension in these cases as the blood pressure is difficult to estimate This is, first, because of the almost invariable presence of auricular fibrillation and second because there is sometimes aortic incompetence, both of which conditions tend to give high readings for the systolic and lower readings for the diastolic pressure In the present cases a minimum diastolic pressure of 100 mm or more was found in 19 (50 per cent) On this criterion of hypertension, it was present in one half of all patients Taking a systolic pressure of 190 mm or more as a criterion of hypertension, it was present in 12 (31 per cent) of cases With either of these standards the incidence of arterial hypertension must be regarded as high in mitral stenosis in the elderly

Yet in spite of this high proportion with hypertension and the advanced average age of the subjects, characteristic anginal pain was experienced by one patient only This was a woman of 71 with mitral stenosis, aortic incompetence, and auricular fibrillation Her blood pressure was 160/100 mm She described typical retrosternal pain in walking up steep hills She had never shown any signs of systemic congestion In a further two patients, however, pain occurred which may be regarded as anginal This was in 2 men who died of left auricular thrombosis and who complained shortly before death of pain in the lower chest and epigastrium

RADIOLOGICAL APPEARANCES

The accepted X-ray cardiac changes in mitral stenosis are an increase in the left middle arc so that the usual slight concavity in this region comes into line with the left lower contour and the shadow of the aortic knuckle, or there is a convexity in this region which may be single or double The vascular pedicle is narrow and the aortic knob is small or non-existent Displacement of the œsophagus

backward and to the right reveals an enlargement of the left auricle At first these changes are not accompanied by any alteration in the shape of the left lower contour or of the right contour but as time passes these also become more or less prominent, and on the right border may be seen a double contour produced by the two auricles

Radioscopy and radiography were carried out in all cases except five, and in three of these five, necropsy was done A cardiac silhouette that could be regarded as within normal limits was seen only once (Fig 1A and 1B) This was in a man aged 58 whose only known attack of rheumatic fever occurred when he was 45 auricular fibrillation was present but symptoms were very mild Slight general cardiac enlargement with increase in the left middle arc was also unusual An example is shown in Fig 2 taken from a man of 53 who had normal blood pressure and whose heart at necropsy weighed 325 g, with moderate right ventricular hypertrophy, the left ventricle being normal The onset of auricular fibrillation causes a rapid increase in the size of the heart even in the absence of systemic

congestion This is shown in Fig 3 and 4 from a woman aged 51 The first of these radiographs was taken while normal rhythm was present and the second a few weeks later after auricular fibrillation had developed, it shows some increase in the right, left lower and left middle contours of the heart Increase in the size of the left auricle sufficient to bring it to the right heart border was seen in five cases although in the first oblique position they usually showed only moderate displacement of the oesophagus Deviation of the oesophagus to the left and backward instead of to the right and backward was met with in two patients (Fig 5, 6, 7, and 8) This is well seen on screening after barium swallow in the second oblique position or in the face position, but in the first position the course of the oesophagus may appear almost normal The narrow vascular pedicle and inconspicuous aortic knob characteristic of the X-ray picture in young subjects with mitral stenosis was never seen On the contrary the knob was always visible and often prominent, though this prominence tends to be minimized by the increased middle arc below it

A　　　　　　　　　　　　　　　　　　B
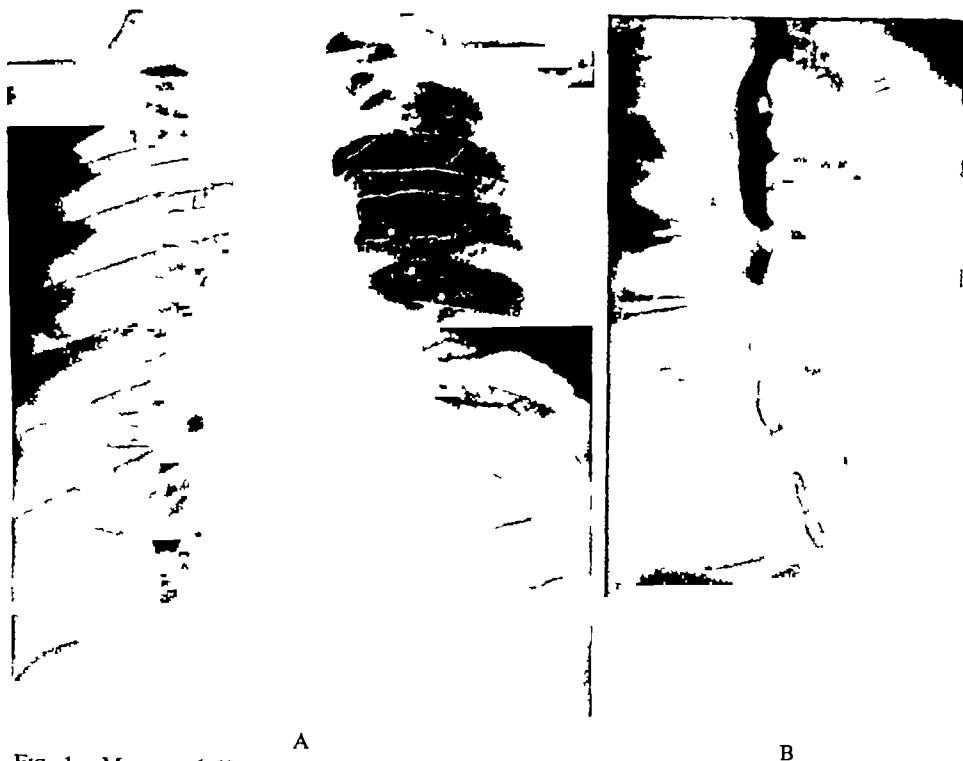
FIG 1 —Man, aged 58, an Army officer on active service until age 56, only known attack of rheumatic fever at age 45, mitral stenosis, auricular fibrillation (A) Postero-anterior radiograph shows heart of normal size and shape, or possibly minimal increase in left middle arc (B) Right (I) oblique view shows no enlargement of left auricle

When the left lower contour is also well out, the result is a contour which bears no resemblance to the typical silhouette of mitral stenosis

A well marked aortic impression on the œsophagus and the opacities of aortic calcification are also common features of the X-ray picture of mitral stenosis in the elderly Fig 9 and 10 represent the characteristic features of mitral stenosis combined with great cardiac enlargement in three women aged 71, 74, and 77 respectively (see pp 162–163)

CAUSE OF DEATH

Sixteen of the 38 patients died after an average duration of symptoms of 4½ years, the average age at death being 62 years   Twelve died with systemic congestion complicated in two by cerebral vascular lesions, acute rheumatism in one and pulmonary infarction in one   Two died from acute pulmonary congestion   In four of the sixteen cases necropsy was done   Two of these showed thrombosis of the left auricle, the thrombus extending on to the mitral valve and further obstructing it   The first, a man aged 60, had some abdominal and leg pains, then developed a sudden painful paraplegia, with pain also in the chest and left arm and delirium There was a complete absence of arterial pulsation in the legs which quickly became gangrenous Death occurred on the 19th day Necropsy showed an extreme mitral stenosis, the orifice just admitting the tip of the little finger   A large soft vegetation measuring 3 cm ×2 cm was situated on the left auricular wall extending on to the aortic cusp of the mitral valve and encroaching on its opening (Fig 11)   Just above the bifurcation of the aorta there was a small dissecting aneurysm of its wall with leakage of a little blood into the retro-peritoneal tissues (Fig 12, page 164)

The second, a man of 53, had lower chest or epigastric pain with symptoms of cerebral anoxæmia a few hours before death   Necropsy again showed extreme mitral stenosis with a loose fresh looking
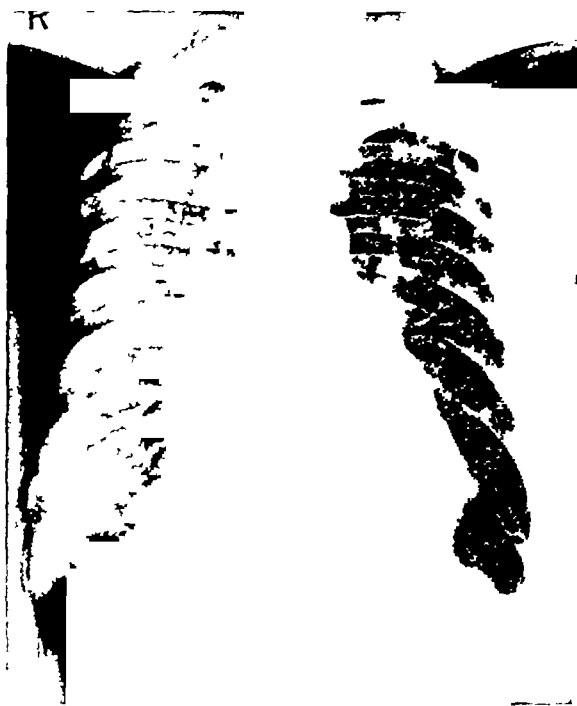
FIG 2 —Man, aged 53   Mitral stenosis and auricular fibrillation   postero-anterior radiograph shows prominence of pulmonary artery and of conus separately, but no prominence of other cardiac contours   aortic knob prominent *Necropsy* severely stenosed calcified mitral valve with fresh thrombus on its auricular aspect, left ventricle not enlarged, heart weight, 325 g

clot blocking the orifice Rough calcified plaques almost encircled the base of the valve Neither of these two patients with severe mitral obstruction had shown signs of systemic congestion Their chest pain near the end may have been cardiac in

TABLE III

CAUSE OF DEATH IN SIXTEEN PATIENTS

(Average age at death 62 years)

Systemic congestive failure	12
(Acute rheumatism 1)	
(Cerebral vascular lesion 2)	
(Pulmonary infarction 1)	
Acute pulmonary œdema	2
L A thrombus obstructing mitral orifice	2

origin and due to auricular thrombosis as suggested by Evans and Benson (1948) In a third case, a woman of 62, necropsy showed pure mitral incompetence The clinical diagnosis had been hypertension and congestive failure, though there was a history of rheumatic fever in childhood, and valve disease had been diagnosed at age 7 The layers of the pericardium were densely adherent throughout the mitral cusps were thick and opaque with rounded margins and the orifice easily admitted four fingers The left auricle was greatly enlarged with a capacity of over 500 ml (Fig 13) A fourth necropsy on a woman of 59 who died in congestive failure shows a heart weighing 750 g with severe mitral stenosis and moderate aortic and tricuspid stenosis

DISCUSSION

The onset of auricular fibrillation appears to mark a turning point in the life history of patients who have suffered little or no handicap from mitral stenosis with normal rhythm up to middle or late life Symptoms are rarely sufficient to make the patient seek advice till an arrhythmia develops nearly always fibrillation, but occasionally it is auricular tachycardia that is responsible for the breakdown Only three patients had normal rhythm when they first came under observation Once fibrillation has become installed the patients' activities are more or less curtailed and their lives must thereafter be lived in a state varying from slight
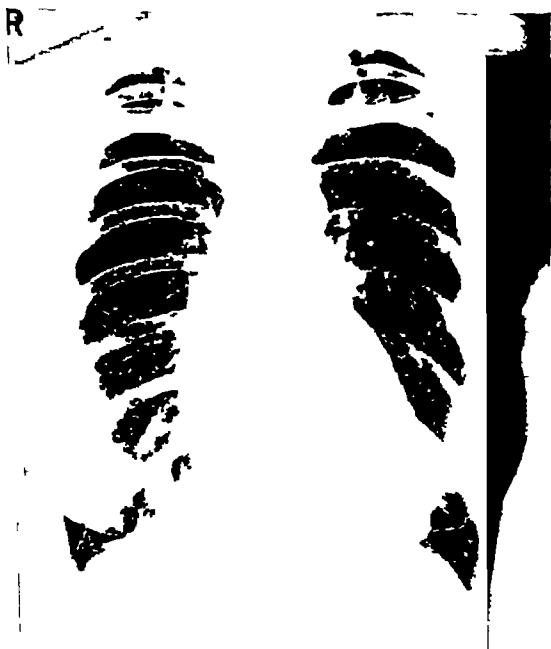
FIG 3 —Woman, aged 51 Mitral stenosis, normal rhythm, radiograph shows some increase in left middle arc only
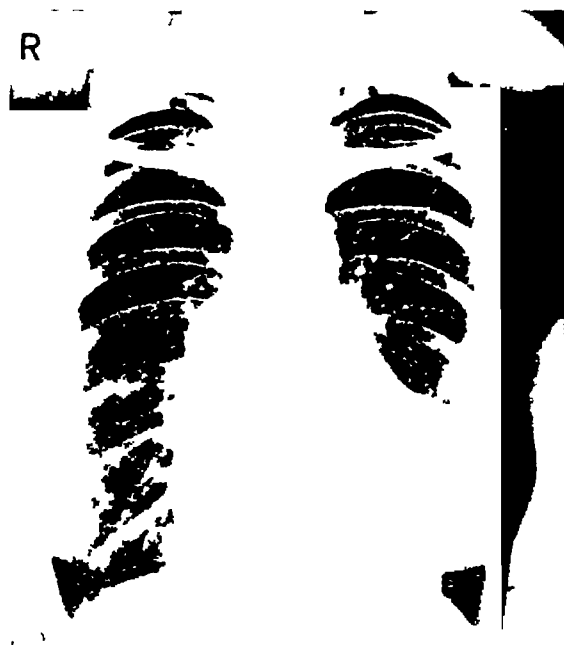
FIG 4 —Same case as Fig 3 Radiograph taken a few weeks later after onset of auricular fibrillation, now shows greater prominence of left middle arc and some increase in left lower and right contours although there were no clinical signs of venous congestion

to severe invalidism At the first appearance of fibrillation with a rapid ventricle or of paroxysmal tachycardia, systemic congestion may occur but this is usually amenable to treatment after which there may be a long period of fair comfort In some cases systemic congestion is delayed for years after the onset of fibrillation but when it does eventually occur it is resistant to treatment Life may nevertheless be prolonged for years in a condition of advanced failure The duration of symptoms that were more or less incapacitating averaged 4½ years for the whole series with extreme for a few weeks to 25 years The commonest cause of death was systemic congestion with pulmonary infarction and cerebral vascular lesions as occasional contributory causes, but in two patients, one with severe hypertension, it was left ventricular failure Two patients who died from left auricular thrombosis are of interest, in that neither had shown systemic congestion in spite of severe mitral stenosis

The radiographic appearance of the heart in mitral stenosis of later life shows some differences from the typical picture in young subjects with this valve lesion, the heart is usually much enlarged and the aortic knob is not small, often it is prominent and shows calcification of its wall Barium swallow sometimes shows a conspicuous aortic impression Left auricular enlargement was revealed by the oesophagogram, yet in cases where the enlargement was great, as indicated by its extension to form part of the right cardiac border, oesophageal displacement in the first oblique position was only moderate In two the oesophagus was displaced considerably to the left and backward Displacement in this direction can be seen only by screening in the second oblique or face positions, it is very rare in mitral stenosis in young subjects

Although a valve lesion or heart disease had been diagnosed in 8 of the patients when they were young, only 3 of the 38 cases described were referred with the diagnosis of mitral stenosis and it seems probable that many elderly patients with this valve lesion are not recognized as such The mitral diastolic murmur often needs careful auscultation for its

FIG 5 —Woman, aged 58 Mitral stenosis, auricular fibrillation, hypertension (260/110), congestive failure, working as domestic servant until a few days previously Postero-anterior radiograph shows great cardiac enlargement, straight left border oesophagus seen through heart shadow, is deviated to left Right pleural effusion
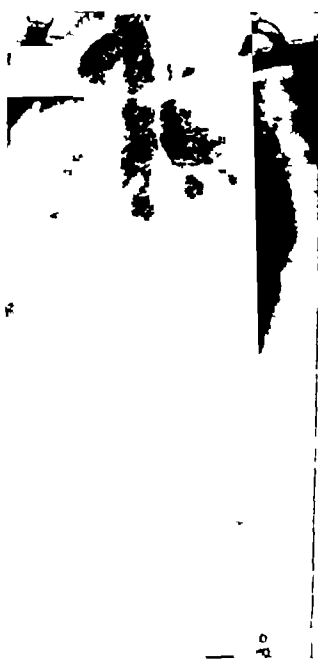
FIG 6 —Same case as Fig 5 Left (II) oblique view, left-auricular enlargement shown by displaced oesophagus
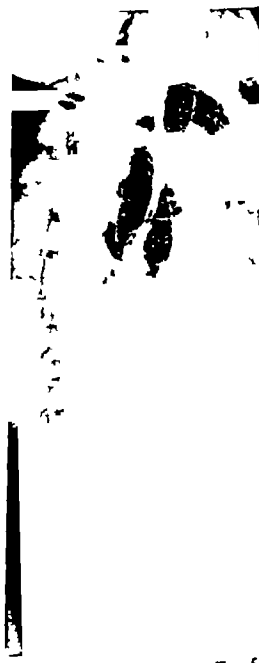
FIG 7 —Same case as Fig 5 and 6 Right (I) oblique view oesophagus not displaced by left auricle but the shadow of the LA can be seen extending backward across the spine Calcification of aortic arch

detection when auricular fibrillation is present and the site of audibility may be very localized Moreover there is a general reluctance to diagnose rheumatic heart disease in the elderly which makes it more unlikely that the characteristic signs will be found Hence a diagnosis of arteriosclerosis or hypertension—which are also frequently present—is made There is little reason to think that an atheromatous lesion with calcification was responsible for any of the present cases and it is not established that such a lesion can produce mitral obstruction of clinical importance In about 60 per cent there was a clear history of rheumatic fever or of a cardiac lesion having been found in early life The absence or mildness of symptoms in the present group until late in life, is perhaps to be accounted for by a relatively slight myocardial injury, in a few perhaps by the first attack of rheumatic fever occurring at a relatively advanced age It is not due merely to the slightness of the valvular stenosis, as indicated by extreme narrowing of the mitral valve in two patients who came to autopsy neither of whom had ever had congestive failure

White and Bland (1941) describe similar severe latent mitral stenosis in three patients aged 73 or more It is evident that as with some other obstructions to the main vascular channels, such as severe aortic stenosis and aortic coarctation, an advanced lesion of this valve is compatible with good health over very long periods of time

SUMMARY

Thirty-eight patients, aged 51 to 77, with mitral stenosis (including one with pure mitral incompetence)are described The valve lesion was believed to be rheumatic in all cases Sixty per cent gave a clear history of rheumatic fever, or of a cardiac lesion having been discovered in early life In a few cases the first known attack of rheumatic fever occurred in the fourth decade or later Physical activity had been little, or not at all, restricted in the past and the appearance of symptoms calling for medical care coincided nearly always with the onset of auricular fibrillation, though occasionally with paroxysmal tachycardia There was arterial hyper-

FIG 8 —Woman, aged 66 Mitral stenosis auricular fibrillation hypertension (245/150) and congestive failure Great general enlargement of the heart, very slight convexity of left middle arc, œsophagus pushed to left by large left auricle deep aortic impression on œsophagus calcification of aortic knob

tension in a high proportion of the patients The X-ray picture differs in several respects from that of younger subjects with mitral stenosis Initial symptoms, occurrence of congestive failure and cause of death are discussed It is suggested that mitral stenosis is not rare in patients over 50 years of age and that careful auscultation of elderly subjects with auricular fibrillation will reveal this valve lesion, where formerly it was unsuspected

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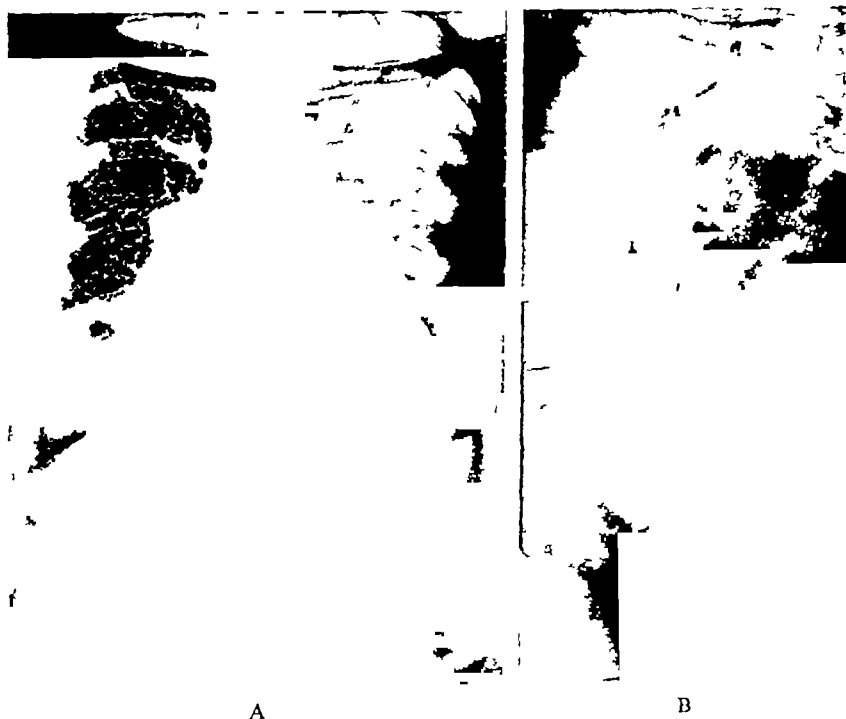
FIG 9 —Woman, aged 71 Mitral stenosis, slight aortic incompetence auricular fibrillation, no signs of systemic congestion, B P 160/100 (A) Postero anterior view shows considerable cardiac enlargement, small convexities on upper part of left profile (B) Right (I) oblique view shows œsophageal displacement by left auricle
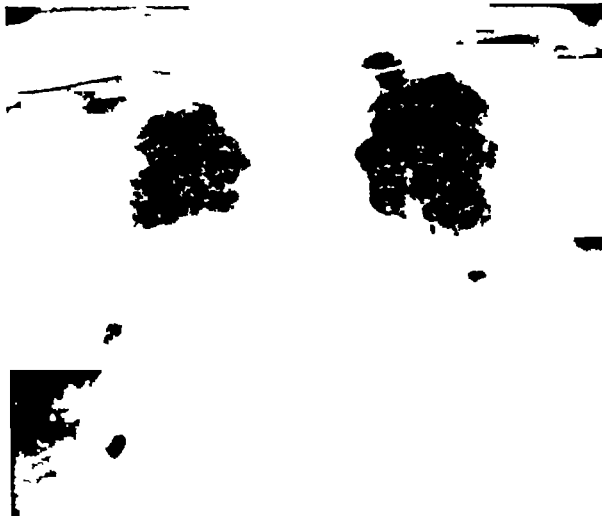
FIG 10 —Woman aged 77   Mitral stenosis aortic incompetence auricular fibrillation congestive failure   Postero anterior view shows very great cardiac enlargement of crinoline shape with a relatively narrow waist above formed by the vascular pedicle, left middle arc very prominent   pulmonary opacities suggesting hæmosiderosis

FIG 11 —Heart from man aged 60   Mitral stenosis auricular fibrillation, no systemic congestion, death from gangrene of the legs   Photograph shows opened left auricle to the left of the specimen, and a thrombus measuring 3 cm × 2 cm on the wall of the auricle which extends on to the aortic cusp of the mitral valve and further obstructs its orifice Mitral opening just admitted tip of little finger

FIG 12 —Abdominal aorta from same patient as Fig 11   Shows perforated atheromatous ulcer just above the bifurcation

FIG 13 —Heart from woman aged 62   History of rheumatic fever in childhood Clinical diagnosis hypertension (215/115) auricular fibrillation congestive failure Necropsy showed adherent pericardium and as shown in photograph large left auricle with a capacity of 500 ml   thickened opaque mitral cusps with rounded margins, the orifice admitting four fingers   This was regarded as rheumatic mitral incompetence without stenosis

CIRCULATION TIMES IN CONGENITAL HEART DISEASE

BY

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Since the introduction of surgical treatment for congenital heart disease, which was mainly of academic interest before, it has become important to diagnose as far as is possible the anatomical and dynamic abnormalities present in each case This need has placed a premium upon any method, more especially if simple and safe, that may help to elucidate the problem The purpose of this communication is to report briefly the results obtained from circulation time estimations in congenital heart disease, and to discuss what value this simple test possesses

References to circulation times are numerous, and it is not intended to review these extensively Blumgart, Weiss, and others first perfected a technique and studied circulation times extensively, reporting their results in 1927 and 1928 Their method involved using radium C and was an objective one, but owing to the technical complexity of the apparatus and agent it is unsuitable for clinical work Most of the methods described subsequently for the arm–tongue time have been subjective, except those using fluorescein, histamine, and sodium cyanide In 1933, sodium dehydrocholate was used in a series reported by Tarr, Oppenheimer, and Sager, although its first use is credited to Nebauer in 1923 Saccharin was introduced by Fishberg, Hitzig, and King in 1933 With the exception of Blumgart's radium method, measurements of the arm–lung time depend upon a subjective reaction, and ether, introduced by Hitzig in 1935 and paraldehyde first used by Caudel in 1938, were the agents commonly used An excellent review of the methods devised was published by Baer and Slipakoff in 1938

References to circulation times in congenital heart disease are scanty, but Tarr, Oppenheimer, and Sager (1933), report that the arm–tongue time, in a patient diagnosed as having Fallot s tetralogy, was on three occasions considerably shorter than normal In 1937, Goldman and McGuire reported the

apparent acceleration of blood velocity as measured by the arm-tongue time in three cases of morbus coeruleus It has been used widely at the Johns Hopkins Hospital, and Taussig (1947) states that the absence of any shortening of the time may support the diagnosis of pure pulmonary stenosis, that shortening of the time may support the diagnosis of Eisenmenger s complex even when there is no obvious cyanosis, and that a prolonged time may be found with aortic stenosis Prinzmetal in 1941, proposed a quantitative method for the estimates of the actual amount of right to left shunt

METHOD USED

The agents used have been 20 per cent sodium dehydrocholate in 18 estimations of the arm–tongue time, and 50 per cent saccharin in a further 22 estimations Saccharin has been used owing to the recent difficulty in obtaining decholin, although this latter gives a sharper and more distinctive end point and has a lower threshold concentration for taste In all 35 estimations of the arm–lung time, 5 per cent paraldehyde in saline has been used The normal range for the arm–tongue time, using these agents, is 11 to 17 seconds, and for the arm–lung time 3 to 8 seconds

Reports have appeared from time to time of unpleasant effects from the use of decholin, and in three cases these have resulted in the patients' death, though in all the reported cases of death, the patients showed a previous history of sensitivity, such as asthma, etc , if patients with such a history are excluded from injections, it seems that decholin is a safe substance to use Saccharin and paraldehyde may cause pain on injection, and the former has been reported as producing abscess formation when injected paravenously Venous thrombosis has been reported as a frequent complication following saccharin and paraldehyde, whilst nausea and vomiting are said to follow the injection of decholin

on occasions In this series there has been no fatality, and no evidence of venous thrombosis or any other complication except that about half the subjects complained of pain in the arm following paraldehyde, whilst one vomited after receiving decholin, and another became extremely nauseated

All patients have been investigated while lying at rest, either in the wards or at the Cardiac Out-patients of Guy's Hospital The injections have been made with the site of injection, in each case a vein at the bend of the elbow, approximately level with the right auricle Four ml of each agent are used, in all-glass syringes fitted with a wide bore intravenous needle After venepuncture has been performed, a minute or so is allowed to pass whilst the local circulatory conditions return to normal in the previously congested area This opportunity is taken of ensuring that the patient knows what to expect, and that he has to signal as he tastes the appropriate substance The time taken for the actual injection has been found to be remarkably constant at 2 to 2 5 seconds, and this can be dis-regarded in the results An assistant is instructed to measure the time taken from the beginning of the injection until the patient s signal Imme-diately following this, the arm–lung time is esti-mated, using the same needle, and merely attaching the second syringe Following the procedure, the patient is instructed to exercise his hand and arm for a few minutes to disperse any paraldehyde that might still be lying in the vein, and so cause throm-bosis

This method is used for the diagnosis of whether a right to left shunt is present or not, but in five cases Prinzmetal s suggested method has been used to assess the percentage of blood shunted from right to left The method consists, briefly, of the measure-ment of the arm–tongue time using successively larger amounts of agent It is only applicable in cases where the shunt does not exceed 50 per cent The theory upon which the method is based postu-lates that any substance arriving in the right ventricle (for example) will proceed along the two alternative pathways tongue and lungs (assuming a shunt to be present), in amounts proportional to the volume of blood passing to those organs There is also a threshold concentration necessary at the taste buds before the subject can appreciate the taste It follows, therefore, that if less than 50 per cent of blood is shunted into the aorta, the injection of increasing amounts of agent will cause a threshold concentration to be reached first in the blood passing via the lungs to the tongue, and hence the first sensation will be noticed in a relatively long, or normal arm–tongue time Subsequently, a con-centration will be reached in the shunted blood that will produce a taste and when this occurs the arm–tongue time measured will suddenly become shortened

If the amount necessary to produce the initial longer time be called A, and that required to cause the sudden change, B, then it can be shown that —

$$\text{Percentage of blood shunted} = \frac{A}{A+B} \times 100$$

In practice the technique is similar in all respects to that previously described, except that amounts increasing by 0 2 ml are injected until first the longer, and then the shorter time is obtained

RESULTS

Of the 36 patients investigated, 35 were suffering from congenital heart disease The remaining patient (always grossly cyanosed, and for 29 years thought to be a case of Fallot's tetralogy) suffered from pulmonary hæmangioma

There were 3 patients with congenital heart disease who were not cyanosed

The average age of patients was 15 years and the range was from 6 to 41 years

Group I Cyanosed Patients in whom both Circu lation Times were Estimated

There were 28 patients, 20 were shown to have a right to left shunt, and in 8 the times were against a shunt Details of these 8 are shown in Table I

The results show failure in 3 (Cases O115, H121, and CB14), and a probable failure in a further one (Case H126) where angiocardiography confirmed the presence of a shunt In the 4 cases at the top of the table the absence of a right to left shunt was confirmed

Group II Cyanosed Patients in whom only the Arm–Tongue Time was Performed

There were 5 patients in this group, and all of these were shown to have a right to left shunt

Group III Acyanotic Patients in whom both Times were Performed

There were 2 patients in this group and neither was suspected clinically of having a right to left shunt, in one a patent ductus arteriosus has recently been ligated (Case O122) but in the other angiocardiography very unexpectedly suggested a right to left shunt (Case C206)

Group IV Patients in whom Prinzmetal s Method was used (See Table II)

TABLE I

PATIENTS NOT DIAGNOSED AS HAVING A RIGHT TO LEFT SHUNT

Reference No	Sex and age	Arm-tongue (seconds)	Arm-lung (seconds)	Diagnosis	Autopsy
(Baker 1949)	M 29	Decholin 14 0	8 5	Lung hæmangioma	Confirmed No shunt
HJ17	F 30	Saccharin 17 5	13 0	Valvular pulmonary stenosis	Confirmed No shunt
P215*	F 20	Saccharin 33 0	22 6	Dilated pulmonary artery + aortic regurgitation	Alive No shunt‡
P212†	F 9	Saccharin 16 7	11 0	Valvular pulmonary stenosis	Confirmed No shunt
H126	F 9	Saccharin 13 0	6 0	? Fallot s tetralogy	Alive Shunt present‡
O115	M 27	Decholin 26 0	15 0	Fallot s tetralogy	Confirmed Shunt present
H121	F 24	Saccharin 17 2	9 2	Fallot s tetralogy	Confirmed Shunt present
CB14	F 13	Saccharin 13 8	8 4	Fallot s tetralogy	Confirmed Shunt present

* Cyanosis of peripheral type   † No cyanosis at rest   ‡ Confirmed by angiocardiography

The result was specially useful in Case P225 as he was not obviously cyanosed at rest the final diagnosis was Eisenmenger s complex It was rather surprising in Case O111 as she too was hardly cyanosed at rest and was thought to have valvular pulmonary stenosis with a patent foramen ovale

Cases 0070 and 0075 were thought to have Fallot s tetralogy

Case 0207 was thought to have valvular pulmonary stenosis and to have developed a right to left shunt later in life This was confirmed at operation and the valve was divided by Mr R C Brock

She made an uneventful recovery, with striking improvement, already being able to walk about the hospital freely, whereas before she had been virtually bedridden It has been possible therefore to compare her circulation times before and after operation

	Arm–Tongue (seconds)	Arm–Lung (seconds)	Hæmo-globin%
Pre-operative	12 2	10 0	122
Post-operative	10 2	6 8	106

The first difference is the overall reduction in circulation times following operation, coupled with an increase in difference between the arm–tongue and arm–lung times The lowering of hæmoglobin which occurred may have helped to shorten the times, but it also seems likely that the partial or complete relief of the valvular obstruction has contributed to this effect, and the reduction in pressure in the right ventricle has diminished the shunt

which had been taking place through the inter-auricular septum

TABLE II

Refer-ence No	Sex and age	Amount producing longer time	Amount producing shorter time	Shunt
0111*	F 8	variable	results	probably 50 o
0075	M 6	0 50 ml	1 50 ml	25%
0070	M 8	1 00 ml	3 00 ml	25%
0207	F 26	1 80 ml	3 00 ml	37%
P225 *	M 13	1 00 ml	5 00 ml	17%

* Cyanosis on exertion only

DISCUSSION

The results presented above have attempted to show that the estimation of the arm–tongue time together with the arm–lung time is a simple and safe method to be used in the diagnosis of the presence of a right to left shunt It is most important that both times be estimated together, and the only satisfactory evidence of a shunt is that they should agree within two seconds of each other This alone can indicate that substances introduced into the right side of the heart reach a point on the great and lesser circuits simultaneously, and there must be a communication between the two before the lung capillaries are reached Further, the blood must be passing from right to left It is important to note that by no means every case of Fallot's

tetralogy or allied condition shows a markedly shortened arm–tongue time, as might be thought, and indeed as the scanty references in previous work report In this series five patients had normal arm–tongue times, though in each case the arm–lung time equalled this, which demonstrates the possible error that may occur if the arm–tongue time is taken alone The chief reason for the failure of the arm–tongue time to be shortened in every case, is probably that the compensatory polycythæmia causes the opposite effect, namely slowing of the time, as shown by Blumgart in cases of polycythæmia rubra vera In the five cases mentioned here it is noteworthy that the hæmoglobin concentration was 140 per cent or more in each It is appropriate to comment upon the disparity in actual values obtained for circulation times, using the methods described above and angiocardiography The normal values stated previously will only hold good if relatively small amounts of agent are introduced into the circulation Experience with angiocardiograms performed on some of the patients used in this series shows that the opaque dye may appear in the aorta two seconds after injection, giving a grossly shortened arm–tongue time This is to be explained by the greater quantity of dye injected, namely 50 ml or more, which consequently causes considerable changes in venous return to the heart

The method has certain disadvantages It is, firstly, a subjective method and the patient's intelligent co-operation is needed This requirement effectively rules out its use in very young children, six years being probably the youngest age at which a satisfactory result may be obtained Since the patients attending a congenital heart clinic for advice will show a high proportion of young children many will not be able to undergo the test Lack of intelligence, even in older persons, apprehension, and general dislike of venepuncture are all factors that have tended to obscure results, and in this series there have been twelve failures from these particular causes

The results show three subjects in whom a right to left shunt was not suspected upon the circulation times, but in whom autopsy had since shown this contention to be incorrect These failures all occurred within a short time of each other, when differing amounts of saccharin to be injected were being tested, and the reason for failure seems to be that too little was used If, as seems reasonable, these patients had a shunt of less than 50 per cent of total, then the injection of too small an amount of saccharin might cause a taste threshold to be reached only by the longer route There is some

support for this, since in the only one of the three cases that had undergone cardiac catheterization, this investigation showed evidence of a moderate shunt only Since these unsatisfactory results, the amount of saccharin injected has been raised, and no further trouble has been encountered

Brief experience with Prinzmetal's method has shown this to be tolerably satisfactory, but a rather higher degree of intelligence and co operation is required The possible errors are great, and it has been found that repetition of the injection of similar amounts does not always produce the same response It is unlikely that accuracy to within less than 10 per cent may be achieved, and in any case, in this context, the method is subject to the criticism that providing the presence of a shunt has been diagnosed, the clinical condition of the patient, reinforced by arterial oxygen estimations is of greater importance in indicating urgency of treatment than a doubtfully accurate estimation of the percentage of blood shunted

SUMMARY

Results of estimating the arm–tongue and arm–lung times in a series of 36 patients suffering from suspected congenital heart disease are given The agents used were 20 per cent sodium dehydrocholate and 50 per cent saccharin for the arm–tongue time, and 5 per cent paraldehyde for the arm–lung time

Reference is made to the complications reported by previous workers, and in this series no reactions of any severity were observed Prinzmetal's method of estimating the percentage of blood shunted in patients known to possess a right to left shunt was used in five cases, and a description of the method is given

The results show that the measurement of the arm–tongue and arm–lung times together is a reliable, simple, and safe method to be used for the diagnosis of a right to left shunt, and failure was encountered in only three cases The reasons for these failures are discussed It is concluded that the single estimation of the arm–tongue time is not a reliable guide to the presence or absence of a shunt The results using Prinzmetal's method show this to be of doubtful value A discussion upon the advantages and disadvantages of the method is given

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MORBUS CŒRULEUS

A STUDY OF 50 CASES AFTER THE BLALOCK–TAUSSIG OPERATION

BY

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The Blalock-Taussig operation for morbus cœruleus was described in February 1945 The position reached in September 1947 was presented to the International Conference of Physicians at that time and has since been published by Taussig (1948) and Blalock (1948a) The steps that led up to this operation and the subsequent developments have been described recently (Campbell, 1948), so will not be referred to further The early results of the first 18 operations at Guy's Hospital, some by Mr Blalock and some by one of us (R C B), have been described (Campbell, 1948), the earlier cases had then been followed for six months

In the present paper we wish to describe the results in the first 50 patients operated on at Guy's Hospital with a systemic-pulmonary anastomosis for cyanotic heart disease, all since September, 1947, by R C B

All the patients were thought to have Fallot's tetralogy or some closely related form of congenital heart disease, except three (Cases 33, 42, and 49), these three had a similar clinical picture, but with left ventricular preponderance in the electrocardiogram, which nearly always indicates tricuspid atresia or stenosis with a non functioning right ventricle (Brown, 1936) The earlier cases have now been followed for from 12 to 15 months and the most recent for 6 months We are not including in the figures that follow 6 patients who have been submitted to operation for pulmonary valvulotomy during this same period

Age incidence Most of the patients were between 3 and 15 and there were rather more boys than girls (28 to 22) One was two and a half years old, 5 were three, 32 were between four and ten, 7 between eleven and sixteen, and 5 (by chance, all men) were between 19 and 27 years of age

Blalock has suggested 3 as the minimum age for operation except in emergencies, and 10 as the ideal upper limit The operative risk is much greater in patients under 3 and there seems more risk that cyanosis will return, perhaps because the anastomosis fails to grow as the child develops Partly because these two risks are not likely to diminish suddenly at 3 years of age, and partly because with the large numbers waiting it seems less harmful to delay operation from 3 to 5 than from say 10 to 12, we have tended, latterly, to make 5 years the earliest age

We have, however, no evidence from our cases that operation is more dangerous or less successful at 3 years of age We do, so far, find it more dangerous in those over 20, but it will be many years before one can avoid the dilemma of operating on older patients with an increased risk, or allowing them to deteriorate and die

SYMPTOMS AND SIGNS

Disability The disability of these patients was extreme many selected for operation were severe cases who were deteriorating and could wait no longer, rather than good operative risks Twenty six were put in the most severe grade (IV) which means that they were made dyspnœic by a few steps and could rarely walk more than 25 yards (Campbell 1948) One of these (Case 43) said he had once walked 100 yards as a great occasion, as he was 13 and attended an ordinary school in his wheeled chair it emphasizes the disability Another 19 were in the next grade (III) which means very severe limitation as they could not play outside without frequent rests and could only walk 50 to 200 yards Three of these, aged 19, 25, and 27, had at one time walked 2 or 3 miles but had become much worse during the last few years

There were 5 who could do something more than this and were placed in grade II, but even they were very incapacitated Two, aged 19 and 16, had been

able to walk one or two miles slowly but were most dissatisfied with being 'unable to do anything' and were enthusiastic for operation whatever the risks The other three were younger and could walk half to one mile on a good day but often they could not do as much as this As further evidence that even these were moderately severe cases, all except one had hæmoglobin percentages between 150 and 126

The large proportion of older patients among the last eight suggests that they had survived because their condition was less severe but was now deteriorating All cases of Fallot's tetralogy have not, of course, such severe disability but the worst have been chosen for early operation

In addition, some of these patients were becoming rapidly worse so that operation was expedited For example, Case 46 attended a second time after three months the distance she could walk had shortened from 150 to 50 yards, her cyanosis and the clubbing of her fingers had become worse The slightest exertion, even dressing provoked almost daily attacks of loss of control of her limbs with semi-consciousness

Our experience suggests that when a patient with Fallot's tetralogy starts deteriorating the prognosis is grave, and several times when this has happened death has not been long delayed

Cyanosis All these patients had been cyanosed from early infancy and all had clubbed fingers The measurement of cyanosis is difficult and is made more so by its quick variation with exertion and temperature In bed in a warm ward many of the patients look so much less blue than as out-patients that they are hardly recognizable With Dr W D Brinton we made some attempts at colour matching but they have not so far been successful The relationship of cyanosis and polycythæmia is reciprocal, the lack of oxygen causing the polycythæmia and this in its turn increasing the appearance of cyanosis

The estimate of cyanosis was made without knowing the hæmoglobin percentage In general terms, those in whom it was from 110 to 129 had been placed in grade II or III as regards their cyanosis, those from 130 to 139, in grade III, and those from 140 to 160, in grade III or IV These and some other details are given in Table I But there was no very close correspondence and sometimes rather surprising contrasts

The cyanosis was generally severe (grade III,* 25 cases) or very severe (grade IV, 15 cases) In 9 it was less than this and often less than would have been expected from the disability, though it was always present even with the patient at rest in

these 9 the hæmoglobin averaged 122 per cent

In one patient in particular (Case 26) where the disability was very great, the cyanosis and clubbing slight and the hæmoglobin 116 per cent, we were somewhat hesitant about operation but the result was just as successful as in others The arterial oxygen saturation was 80 per cent falling to 75 per cent with very trivial leg movements (Dr Zak) If the disability is severe enough, relatively slight cyanosis should not as a rule be a contra-indication to operation

Onset of cyanosis The age from which cyanosis was first noticed is of great importance Naturally, if there is an over-riding aorta and a ventricular septal defect, venous blood will be passing into the aorta from birth or soon after Cyanosis may be noted at once depending on the amount of shunt, and will become more obvious as greater demands are made on the circulation and as polycythæmia develops It is most important not to mistake temporary cyanosis *at birth* for cyanosis that has persisted *from birth*

Cyanosis was noted from an earlier age than 18 months in all except one The actual figures were from birth or soon after in 30 of the 50, from between 2 and 6 months in 9, from between 7 and 10 months in 6, from between 15 and 18 months in 4, and at 24 months in Case 32

Of the 5 where cyanosis was not noted till after 15 months, 4 seemed ordinary cases of Fallot's tetralogy though one lived to 27 the fifth (Case 32) had pulmonary stenosis and transposition of the aorta so that cyanosis might have been expected from birth It is strange, but can hardly be more than a coincidence, that 3 of these 5 patients died after operation

Polycythæmia The hæmoglobin percentage varied from 110 to 160 and averaged 137 The highest figures were 160 (Case 35), 158 (Case 29), 157 (Case 6), and 153 (Case 22) All these except the first looked severely polycythæmic

The red blood cells were generally between 6 0 and 9 0 and averaged 7 8 millions, but in two it was 11 6 and 11 1 millions (Cases 41 and 47), the next highest being 10 1 million and several of 9 0 million or just over Curiously enough these two had not specially high hæmoglobin percentages, the figures being 140 and 137 so that the colour indices were unusually low—0 58 and 0 60 respectively

The hæmatocrit reading was generally between 60 and 85 and averaged 74 As might be expected, it generally agreed more closely but not very closely with the red cell count The highest readings were 94 (Case 41, one of the highest red cell counts), 92 (Case 29, one of the highest hæmoglobins), 88, 87,

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* Grade III Cyanosis moderately severe *at rest* and obvious at a glance Grade IV Cyanosis gross, *at rest*

TABLE I

CASES OF MORBUS CŒRULEUS SUBMITTED TO BLALOCK-TAUSSIG OPERATION AT GUY'S HOSPITAL

Case No	Initials	Sex and Age	Cyanosis	Disability	Hæmo globin (percentage)	Red cells (millions)	Hæmatocrit	Hæmoglobin 3 or 4 weeks after operation	Reference No
1A	A C	M 19	4	3	148	10 0	78	Died	P01A
19	S F	M 4	2–3	3	112	6·0	58	100	CB04
20	M E	F 5	2–3	3	110	5 9	63	100	0018
21	T G	M 4	3	3—	138	8 0	(68)	127	C004
22	M L	F 13	4	4	153	7 2	87	N C *	C005
23	D S	M 19	4	4—	130	6 0	77	106	0015
24	C M	F 6	4	4	148	8 8	81	128	0019
25	J R	F 6	2–3	4	140	7 4	70	101	0005
26	J L	M 15	2	4	116	8 4	57	88	P069
27	D F	F 10	3+	3	150	8 0	83	N C	0027
28	J L	F 3	4	4	107	6 6	64	N C	H113
29	T H	M 10	4	4	158	8 2	92	122	0036
30	G F	F 7	3—	3—	133	8 0	72	—	P045
31	V S	F 2	2–3	2–3	136	7 4	72	110	C008
32	J H	M 11	3—	4	144	8 0	74	Died	P054
33	P S †	M 4	3	4	132	9 2	85	109	0022
34	A W	F 9	3	2+	118	6 4	63	97	H128
35	M C	F 7	3	4	160	7 9	67	Died	P037
36	P R	F 16	2+	2+	126	5 3	58	89	C007
37	J W	M 5	4	4	136	8 4	81	103	P102
38	C B	F 7	3—	4	142	10 1	81	Died	H106
39	P C	M 10	3	3	139	8 3	87	114	CB09
40	D S	M 5	3+	3	140	7 7	71	105	P089
41	J H	F 5	4	4	140	11 6	94	115	CB17
42	S H †	M 19	3	2+	144	8 0	—	112	P057
43	T H	M 13	3	4	142	7 2	69	—	P056
44	G S	F 11	4	4	142	8 6	84	110	H120
45	S N	M 3	2	4	109	6 6	—	92	0017
46	K C	F 15	3	4	135	8 9	76	—	0105
47	G K	M 11	3	3	137	11 1	—	115	0184
48	R B	M 27	4	3	144	9 1	85	Died	0115
49	J C †	M 8	4	4	125	8 6	73	123	0007
50	M S	F 13	3	2+	138	7 2	—	110	0140

* N C = No change as no effective anastomosis   † Tricuspid atresia

Cases 1–17 have been described previously (Campbell, 1948)

and 86, several others were very close to this

As would be expected, the red cell count increases regularly with the hæmoglobin percentage in the lower ranges, but to our surprise this parallel increase is not continued in the higher ranges In Table II the cases have been classified according to the hæmoglobin and it will be seen that the red cells and hæmatocrit increase as the hæmoglobin goes up from 112 to 134, but there is no further increase either in the red cells or in the hæmatocrit as the hæmoglobin goes up from 134 to 153 The disadvantages of a red cell count over 8 0 million may produce some mechanism in the body that prevents a further rise, but if so the two cases with counts over 11 0 million are all the more surprising

Apparently as the hæmoglobin rises above 130 per cent the red cell count and hæmatocrit do not on the average rise further with the result that the colour index rises towards unity

Clubbing of the fingers and toes All these cases showed moderate or severe clubbing of the fingers and toes, and Case 26 (whose hæmoglobin was 116 per cent) was the only one who did not have the complete picture as he had curvature of the nails without any noticeable broadening Fifteen were marked as having moderate rather than severe clubbing and these included 8 with hæmoglobin percentages of from 110 to 126, but the others were about 140 Six were marked as having unusually severe clubbing their hæmoglobin ranged from

TABLE II

AVERAGE BLOOD COUNTS GROUPED BY THE HÆMOGLOBIN LEVEL

Hæmoglobin		No of cases	Average red cell count (millions)	Average hæmato crit	Average colour index
Range	Average				
110–119	112	8	6 5	62	0 86
120–129	124	4	7 2	63	0 86
130–139	134	12	8 3*	77	0 81*
140–149	145	16	8 2	80	0 88
150–160	153	10	7 9	76	0 97
110–129	116	12	6 7	63	0 86
130–160	144	38	8 1	78	0 88
All cases	137	50	7 8	74	0 87

* Without the two cases with counts over 11 0 million these figures would be 7 8 and 0 85

130 to 160 per cent This correlation between clubbing and polycythæmia might be expected Fig 1 and 2 show severe clubbing of the same fingers a year after operation when the degree of clubbing has become much less

Squatting Of these 50 patients, 41 had a history of squatting and 7 gave no such history, there were 2 with no information Fig 3 illustrates the typical position Taussig considers squatting almost constant in Fallot s tetralogy, but our evidence is against this though we find its does occur in about 80 per cent It seems unlikely that the diagnosis was wrong in 7 who were not squatting One had tricuspid atresia (Case 42) and the operation was as successful in him as it was in 3 others who did not squat (Cases 5, 10, and 36) It is curious, but again perhaps no more than a coincidence, that 3 of the relatively small number of unsuccessful results (Cases 11 22, and 27) occurred among this small number of non squatters

Mental and physical development It is surprising that the mental development should be so good, considering the severity of the anoxæmia All but two of these children were normal or often above the average although, of course, many were educationally backward We have used the age of walking and talking as rough measurements

Generally the child walked at a normal age but a few were late Most children (33 cases) started walking at or before two years but it was delayed in 12 till three years in 2 till four years, in 1 till five years, and in 2 till seven years There was no mental defect in these children and the last two boys seemed of average or more than average intelligence

Most children (38 cases) started talking at a
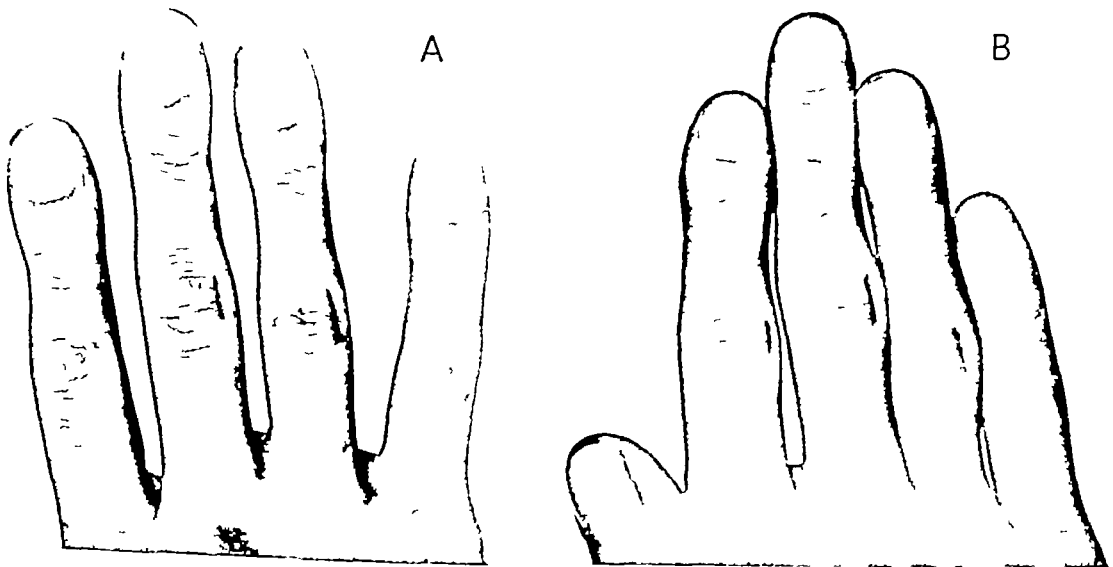
FIG 1 —Clubbing of fingers and its disappearance after operation. This position shows the disappearance of the broadening from side to side and some diminution of the curvature With moderate clubbing it may disappear completely in five or six months but with a more severe grade such as this something is left permanently and the illustration is nearly a year after operation Case 23
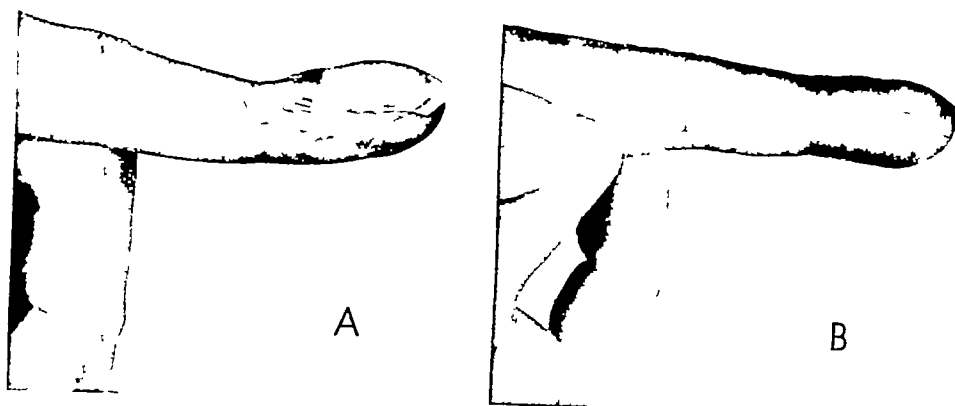
FIG 2 —Clubbing of the fingers before and a year after operation, showing diminution of the broadening from front to back and of the curvature, and a more normal appearance of the skin   Case 23

normal age, generally between 12 and 18 months Seven were said to have been able to talk at two years, 2 at two and a half years, and 3 at three years

Only 4 (Cases 19, 28, 35, and 49) were slow both in walking and talking   Case 19 was mentally backward and Case 35, who had a cataract also, following maternal rubella during pregnancy, was rather backward   All the others were normal mentally

Most of the children were under weight and their parents always complained of difficulty in getting them to eat   On the average they were only slightly under height so that their thinness was very obvious Often the chest was badly developed with some tendency to pigeon chest and to a Harrison's sulcus The veins over the chest were often more visible than normally

PHYSICAL SIGNS

The heart is generally of normal size and anything more than very slight enlargement should raise a suspicion that the lesion is not Fallot's tetralogy or is complicated by the addition of some other defect   The size and shape is dealt with more fully in the section on radiology

Systolic murmur and thrill   There is generally a *systolic murmur* in the second, third, and fourth spaces on the left, becoming fainter towards the apex   The murmur is often loud enough to be conducted widely, sometimes to the right side or to the back   Sometimes the pitch of the murmur differs over the pulmonary area and lower down in

the fourth left space and this may be due to there being two different murmurs produced by the pulmonary stenosis and by the ventricular septal defect

The loudness and harshness of the murmur varies a great deal   There were 4 cases where no systolic murmur was heard (Cases 9, 22, 41, and 48), all were of severe degree and in the last, who died, there was a calcified pulmonary valve   In 2 of these 4 and in 2 others, triple rhythm with an addition of a third heart sound was so obvious as to be almost the main physical sign   It was equally common for the murmur to be described as soft or faint (13 cases), as average (13 cases), or as loud, rough, or harsh (14 cases+6 special cases)   The 6 special cases with a harsh or rough murmur were the 3 with tricuspid atresia, Case 28 with a large pulmonary artery, and Cases 32 and 35 with unusual features discovered post-mortem (see page 192)

Such a harsh or rough murmur (or thrill of well marked intensity) is, therefore, a reason for considering carefully if the diagnosis is correct, though it may be found fairly often in an ordinary case of Fallot's tetralogy, perhaps indicating that the stenosis is fairly severe, but not that there is atresia, when a murmur may be absent

In none of these cases was any diastolic murmur heard, but some others with the features of Fallot's tetralogy and a diastolic murmur have been deferred for fuller investigation

A *thrill* was present in more than half, but generally it was faint and might only be felt at times or after exertion   It was usually maximal

Fig 3 —Case 33 with tricuspid atresia and non-functioning right ventricle A
typical position adopted in squatting, though in many of the older patients
the knees are brought still closer to the chest

in the pulmonary area but occasionally towards the apex As would be expected it was closely correlated with the harshness of the systolic murmur The thrill was never of great intensity, it was of moderate intensity in 13 cases, but this included the 3 with tricuspid atresia and the 2 with unusual findings post-mortem It was difficult to feel or only felt occasionally or after exercise in 17 cases No thrill was felt at the many examinations in 20 cases

Pulmonary second sound Auscultation should be carried out with the patient sitting up and lying down and during each phase of respiration, before a decision is taken about the intensity of the second sound

Diminution of the second sound in the pulmonary area has been traditionally regarded as an important sign in the diagnosis of pulmonary stenosis As far as Fallot's tetralogy is concerned this is not so, the second sound is generally normal and is as likely

to be a little increased as diminished   It was often as loud on the left as on the right side at the base

Any great increase, however, is likely to indicate that the pulmonary pressure is raised and that on screening a large pulsating pulmonary artery will be seen and that the lung fields will be congested instead of clear   This is specially true if the second sound has a drum-like quality   Visible pulsation in the pulmonary area, and palpable diastolic shock also suggest that the lesion is not Fallot's tetralogy and that the pulmonary pressure is raised   We would emphasize that the significance of the change in the pulmonary second sound depends on a sound that is *much increased* and not to one that is *slightly increased*

In these 50 cases it was recorded as normal in 17, as diminished in 11, and as slightly increased in 13, in 9 it was more notably increased   These 9 included one where the pulmonary pressure was high (Case 28), one with tricuspid atresia (Case 42), one with severe cyanosis who was hardly helped by operation (Case 22), and one who had infundibular stenosis and a transposed aorta (Case 32), but the other five seemed ordinary cases who were helped by operation

No case of Fallot's tetralogy has had a drum-like pulmonary second sound, even if the pulmonary artery was more prominent than usual   A diastolic murmur immediately after this sound was never heard in Fallot's tetralogy though both these findings are not uncommon in other types of cyanotic congenital heart disease

Blood pressure   The blood pressure in these cases averaged 106/73, though sometimes it was hard to get an accurate diastolic reading   In nearly every case it was within the range 115–95/80–65 and in 4 cases where it was about 127/90, all were over 15 years of age   In some of the older patients it seems to be increasing a little, still with a small pulse pressure

RADIOLOGY OF THE HEART

In the account of the first 18 cases (Campbell, 1948), the size and shape of the heart was discussed at some length and the difficulty of describing any characteristic shape was emphasized   Less than half had hearts that were sabot shaped and the other half had more normal shaped hearts, sometimes with a gross hollow pulmonary bay, but often with an almost straight left border or occasionally even with some slight prominence in the region of the pulmonary conus   The findings are much the same in the present series and we are not discussing the question further

We would, however, emphasize three negative points as of the greatest importance

The density of the lung   The most decisive—and perhaps the most decisive point in the diagnosis of a condition that can be helped by systemic pulmonary anastomosis—is the absence of noticeable pulsation in the lung roots, with an absence of density in the lung fields as a whole

The size of the heart   The second important point is the size of the heart   In most cases of Fallot's tetralogy, however great the disability and cyanosis, the heart is of normal size or even smaller   Anything more than trivial enlargement of the heart makes one hesitant about operation, partly because it suggests that there are greater complications in the congenital abnormality, and partly because the heart is less able to stand any enlargement that may follow the creation of an artificial ductus arteriosus   This is discussed more fully in the next section

The pulmonary artery   The third point, of almost equal importance, is that there should be no undue prominence of the pulmonary artery and better still, that there should be a striking hollow in the pulmonary region, though as already stated, some patients have a rather straight left border   There may even be a convex projection in the region of the conus just below the origin of the pulmonary artery due to the prominence of the infundibulum distal to the infundibular stenosis   Or there may be a dilatation of the pulmonary artery beyond a pulmonary valvular stenosis but this is rare with Fallot's tetralogy, and should show no pulsation

It is desirable that one should be able to see both pulmonary branches, because then a pulmonary vessel is available for the anastomosis and there is no risk of the patient dying suddenly from arrest of the pulmonary blood flow when one pulmonary artery is clamped   This accident occurred in Case 17, in Case 27 no operation was possible because the pulmonary artery was too small   Looking back at the X-ray films we think that in the latter, it should have been possible to tell this before operation, but in the former it would not have been easy, as there was relative density round the lung roots, presumably owing to the collateral circulation

In many cases, the hollow in the region of the pulmonary artery in the P–A view and the large aortic window in the left oblique, together with the absence of pulsation and the absence of density in the lung fields, make the diagnosis easy after radioscopy, and there seems no need for any further investigation   In others the prominence of the pulmonary artery and the density of the lungs with or without pulsation far out in the lung fields at once makes it obvious that the patient is not suitable for operation   But there remain others where the decision is difficult, the density produced by the

collateral circulation causes one of the greatest difficulties but here there is no pulsation and more pin point scattered shadows Our first mistake in this direction was in Case 28 where we had been doubtful about the prominence of the lung fields but had decided there was pulmonary stenosis However at operation the pulmonary artery was found to be large and pulsating with a pressure well over 80 mm of mercury This was in a child who was unable to stand and had been screened lying down

The right (I) oblique position on radioscopy will help in showing if there is any undue prominence or pulsation of the pulmonary artery or of its left branch The left (II) oblique will define the relative size of the ventricles and will generally show the left of normal size with the right somewhat but generally not greatly, enlarged It also helps to show the size of the pulmonary artery and of the aorta

The aortic arch A barium swallow is necessary to determine whether the aortic arch is on the left or right As the barium is swallowed it is often of help to keep ones eyes fixed on the aortic knuckle, as the barium may sometimes follow a preliminary curve to the right before it reaches the aortic knuckle and if this is small it may be missed It is hardly necessary to say that the barium should be of thick consistency

The aortic arch was right-sided in 14 and left sided in 36 of the cases which is nearly the usual proportion of 1 in 4

THE SIZE OF THE HEART

The heart size is not easy to estimate with accuracy, and general opinion ranks inspection of the film and still better, of the heart on radioscopy, as a better method than any specific measurement

The following estimates of the heart sizes have been decided by one of us (M C) in retrospect, mainly on the P-A films, because these are easiest for comparison from case to case and were always available Some attention was paid to the cardiothoracic ratio (c t r) in each but the decision was made mainly on the general appearance It is therefore, interesting to see how these estimates compare with the c t r which are more useful for conveying an idea to others They are given below against the estimated size of the heart, the figures in brackets refers to the number of cases

Very small	
Small	37–43 (4)
Small normal	41–49 (10)
Normal	45–50 (5)
Large normal	45–52 (15)
Enlarged	49–54 (8)
	52–61 (8)

In 14 cases the hearts were regarded as small and in 8 only as enlarged, though possibly some people might have counted the 8 " large normal ' as enlarged the remaining 28 (or 20) were regarded as of usual size

The 8 that were enlarged will be discussed in more detail, and taking them from the largest downwards they were as follows

Case 35 (c t r 62) died after operation and there was a single auricle as well as the other features of Fallot s tetralogy

Case 33 (c t r 61) had tricuspid atresia with a non functioning right ventricle and although the operation has been most successful and the patient is able to lead a life quite unlike anything previously, the heart has subsequently enlarged more than we like

Case 28 (c t r 56) had some doubt about the lung fields before operation and at operation the pulmonary artery was found to be large with a high pressure and the patient probably had Eisenmenger's complex

Case 11 (c t r 55) was not helped by operation but we thought this was due to technical difficulties with the anastomosis and did not indicate a wrong diagnosis

The next four fall into a category of slighter enlargement

Cases 8 *and* 47 (c t r 52 and 53) seemed to be ordinary cases of Fallot s tetralogy and the operation was satisfactory, Case 8 being 25 years old

Case 48 (c t r 52) was an ordinary case of Fallot s tetralogy who died after operation, he was 27

Case 32 (c t r 52) had the aorta arising from the right ventricle and he, too, died after operation It will be seen that among these 8 cases there were several where the diagnosis was more complicated than straightforward Fallot s tetralogy or where the patients did not do well, and the greatest care should be exercised in chosing any patient with significant cardiac enlargement

There were four other patients where we decided to call the heart large normal, though it was difficult to be sure it was not slightly enlarged it was interesting that the c t r were much the same as the four just described, where we thought there was enlargement

Cases 45 and 30 (c t r 54 and 53) seemed to be ordinary examples of Fallot s tetralogy and did well after operation Case 38 (c t r 53) who died after operation had Fallot s tetralogy and Case 49 (c t r 52 5) had tricuspid atresia and did well after operation As three of these did well and there is no reason to think that the one death was due to the heart size, it is probable that similar cases can reasonably be included as suitable for operation
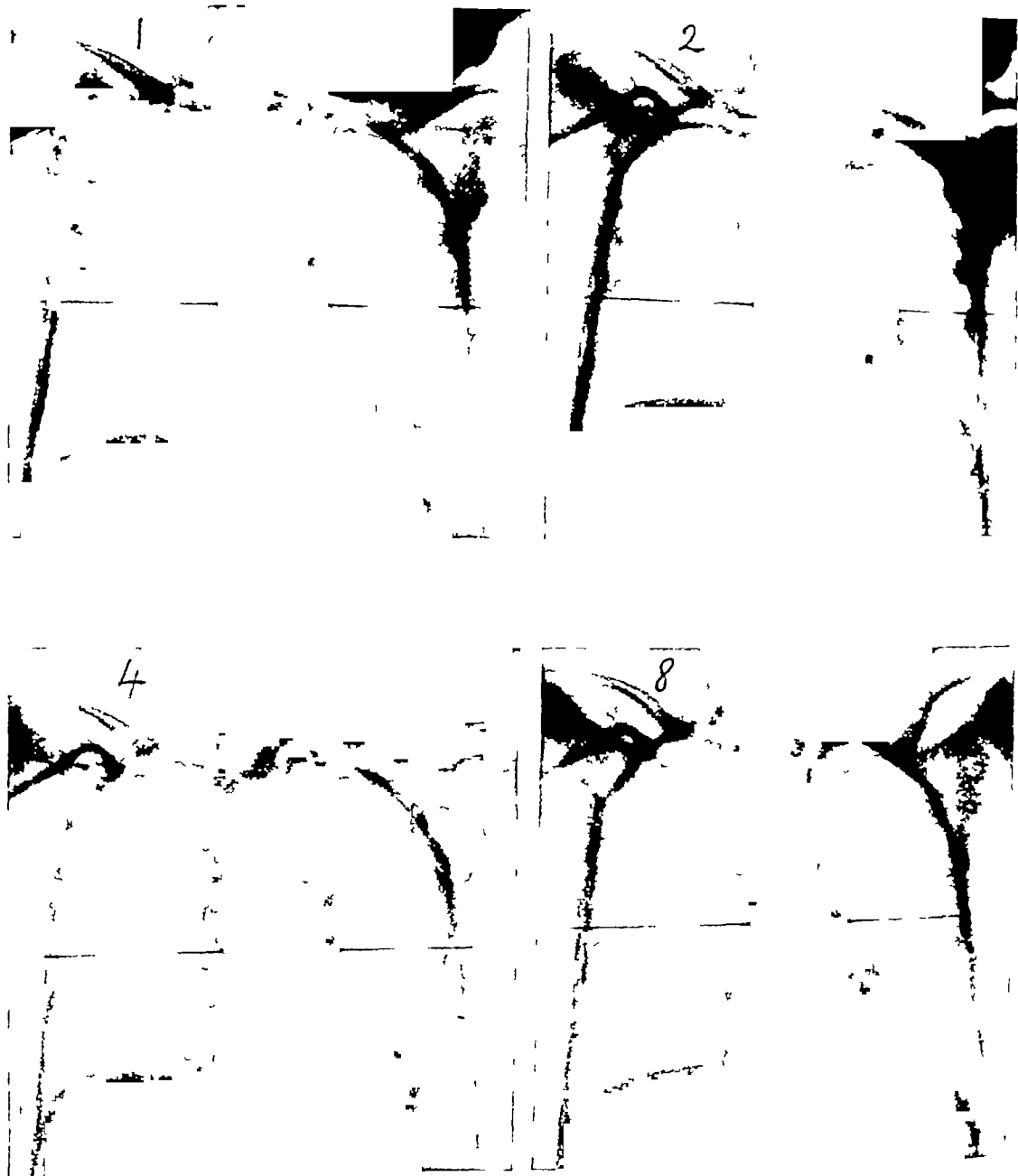
FIG 4 —Case 39   Fallot's tetralogy   The film at 1 second shows normal filling of the right auricle   The film at 2 seconds shows striking filling of the large aorta arching to the right and some filling of its branches   There is evidence of filling of the left ventricle   There is no significant change in the pulmonary arteries   The film at 4 seconds still shows the aorta but less clearly and the subclavian more clearly   The filling of the pulmonary arteries is trivial but this was the maximum reached   In the film at 8 seconds the shadows are fading though the aorta can still be seen   The pulmonary arteries and the lungs as a whole are lighter than at 4 seconds   The conclusion is a large right to left shunt with a right-sided aortic arch and a fairly severe pulmonary stenosis
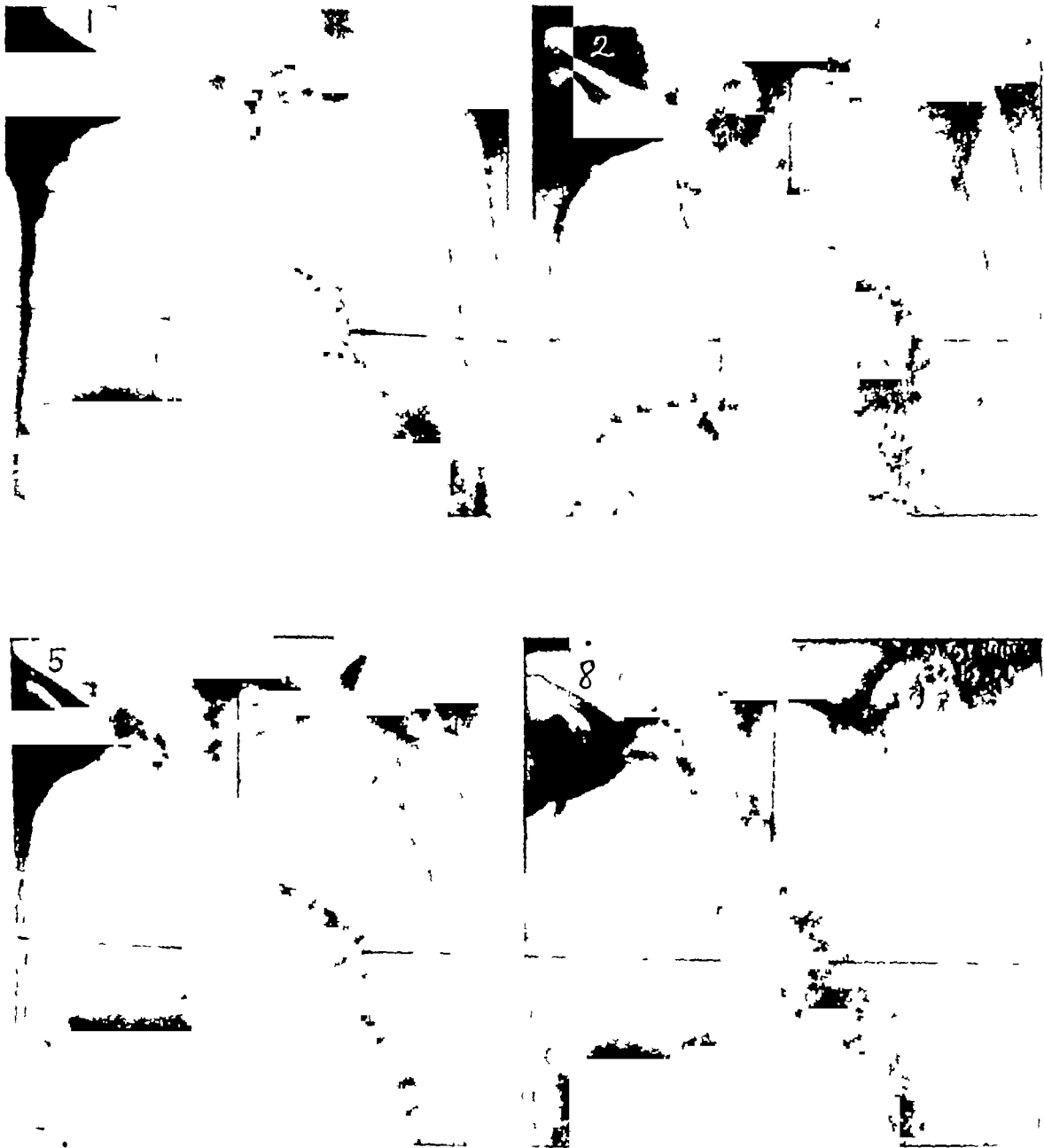
FIG 5—Case 47   Fallot s tetralogy   The film at 1 second shows normal filling of the S V C   and right auricle
The film at 2 seconds shows dense filling of the right ventricle and of the aorta arching to the right and of its
branches as far as the subclavian in the left axilla, indicating an aorta in free communication with the right
ventricle, the dye has not passed out to the borders of the left ventricle   At the same time, the pulmonary arteries
have begun to fill   The film at 5 seconds has been chosen because it shows as much pulmonary filling as at
any time and obviously little blood has entered the lungs   The degree of filling is a far better indication of
pulmonary stenosis than the time at which dye can first be seen in the pulmonary arteries   The right ventricle
and aorta are clearing   The film at 8 seconds shows that the heart as a whole is becoming clearer   The
conclusion is a large right to left shunt with a moderate degree of pulmonary stenosis

and that if the heart can be passed as not much enlarged a relatively high c t r is not a reason for deciding against operation

We have no example to report of a successful operation in a patient with Fallot's tetralogy with the c t r. over 55 But this may be partly due to selection of patients who had not the larger hearts, and this is a question that still needs more experience We are glad we did not exclude the boy with tricuspid atresia with c t r of 61 but whether his improvement can last as long as in some of the others remains to be seen

From our present experience and from the tables of Lincoln and Spillman (1928), of Maresh and Washburn (1938), and of Caffey (1945) it seems that under the age of 2 years the c t r averages 49 and varies between 40 and 65 (60 after one year) in normal children These figures do not concern our present purpose directly but may help in advising parents whether their children may possibly be helped by operation later

From 2 to 5 years of age the normal range lies between 43 and 52, and from 6 years onwards the average c t r falls slightly from 47 to 45, with a range from about 40 to 50 The original figures of Danzer as long ago as 1919 gave 39 to 50 as the adult range with an average of 45, he stated that a c t r. of 52 might be normal if the heart did not look enlarged, but that one of 53 was pathological These last figures were of course concerned with adults but seem to agree with our conclusions

On our present experience, we consider that a heart which seems a little enlarged with the c t r of 52 to 54 should certainly not contraindicate operation, though a larger heart than this often indicates the presence of some complication and is probably a bar to *lasting* improvement We have not yet sufficient evidence to say how often operation should be advised in these larger hearts for the sake of immediate advantages

ANGIOCARDIOGRAPHY

We do not propose to discuss in detail the help that can be obtained from angiocardiography which was only available in nine of the later cases of this series As a rule, there should be no need for this help from the point of view of diagnosis, but in border line cases where a heavy collateral circulation hides the diminished blood supply to the lungs, it may be of the greatest value, and it may help to establish the diagnosis in complicated cases where no diagnosis can be made on clinical grounds alone Apart from this, it has proved of increasing value from the surgical point of view in delineating the anatomical arrangement of the arterial branches

from the aorta and of the size and position of the pulmonary arteries

As Fig 4 and 5 show, there is no difficulty in demonstrating the shunt from the over-riding aorta and this is generally well seen in the film taken at the 2nd second in cases of Fallot s tetralogy Often the pulmonary arteries start filling at the same time, which might suggest there was no great degree of pulmonary stenosis but we have found that the amount of the increased density of the lungs during the subsequent 5 seconds is a better test than the speed with which the opaque substance can first be seen in the pulmonary arteries Even so, angiocardiography seems to give an added precision to the assessment of the degree of pulmonary stenosis present in different cases of Fallot's tetralogy, and may help in distinguishing between valvular and infundibular stenosis Both these points may ultimately be useful in deciding the sort of operation that is most likely to be successful

ELECTROCARDIOGRAMS

The two most striking features of the cardiogram are the large pointed P wave especially in lead II and the right ventricular preponderance This is of such a degree that we think the term ventricular preponderance rather than axis deviation is justified even on the standard leads We hope to deal later with the value of unipolar chest leads as these were not available for all the early cases

Wood and Selzer (1939) thought that a tall spiked P wave might be produced by a right auricular hypertrophy Pardee (1941) accepts the view that abnormally high pointed P waves occur with hypertrophy of the right auricle, while notching and broadening are seen with hypertrophy of the left auricle

The prominent pointed P wave was generally tallest in lead II and some examples are given in Fig 6 The width of the P waves was generally 2 mm and exceptionally up to 3 mm In these 50 cases P II varied from 2 to 8 mm in height, generally between 3 to 7 mm Once (Case 30) it was small and sharply inverted There was only one other where P II was as small as 2 mm high, 10 cases where it was 3 mm high, 16 where it was 4 mm 11 where it was 5 mm , 6 where it was 6 mm , 4 where it was 7 mm and 1 where it was 8 mm high The average was 4 5 mm Chamberlain and Hay (1939) give 1 5 mm as the average size of P II in the first decade with a maximum of 3·0 mm Pardee (1941) gives 2 to 5 mm as the usual size for the large P waves of mitral stenosis

The cause for these large P waves is not certain It is not due to the tachycardia that is generally

A B C D E
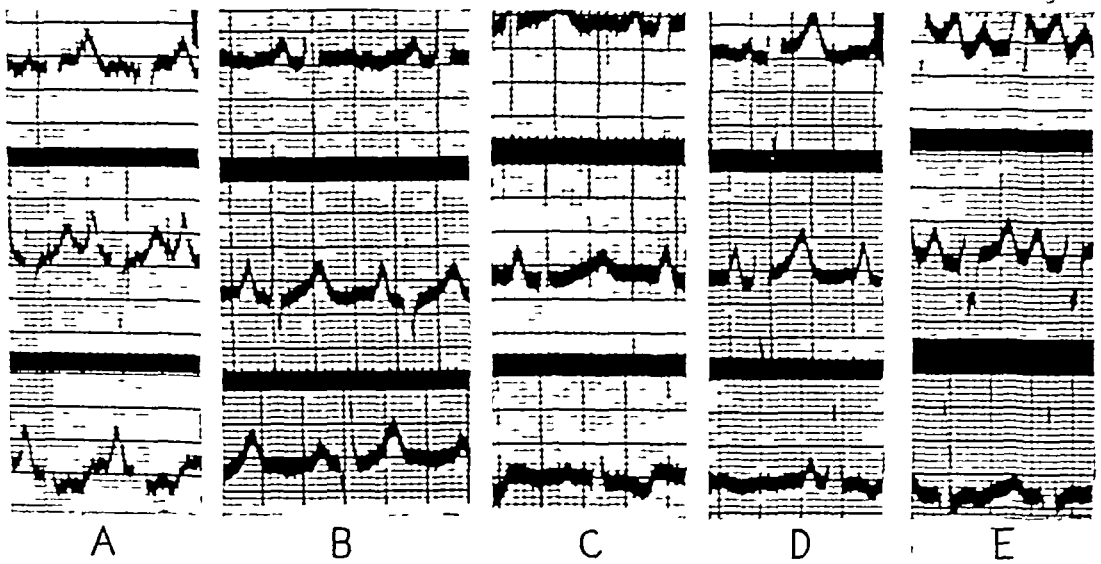
FIG 6 —Typical electrocardiograms from 5 cases of Fallot s tetralogy showing gross right axis deviation and large pointed P waves (A) from Case 0208 confirmed post mortem (B)-(E) from Cases P067, H120 P022, and P035 confirmed by a successful result of operation for a systemic pulmonary anastomosis (Reduced to five sixths)

present, especially in the younger patients as equally tall P waves occur in the same subject when the rate is slower The variability suggests that it is partly due to strain on the right auricle as well as the hypertrophy which should make for greater constancy Moderately large and pointed P waves may occur with cardiac infarction or in cor pulmonale where there is right heart strain Large P waves were seen equally in the cases of tricuspid atresia

In Case 35 where there was a single auricle the P wave was large and pointed, 5 mm high In Case 49 with tricuspid atresia it was tall and bifid as well In the other two cases with tricuspid atresia the P wave was sometimes large and broad in Case 42, but in Case 33 it was not remarkable Occasionally the P waves may show a fair amount of variation in height in the same record (e g Case 35) Where more than one cardiogram was taken before operation the P waves often differed in amplitude but never to any great extent except in Case 36, although there were large pointed P waves in her first cardiogram with a rate of 115, a subsequent one done six months later, but before operation, showed normal small P waves, with a rate of 75, there were no other significant changes in the two curves

The most significant finding as one might expect was the high degree of right ventricular preponderance The main exceptions were the 3 cases with left ventricular preponderance, it is fairly certain

that such a case will turn out to be tricuspid atresia or stenosis with a non-functioning right ventricle especially if on radioscopy the left is the larger of the two ventricles

In the 47 cases that were thought to have Fallot s tetralogy, the general finding was an absent Q, a diminutive or very small R and a large S in lead I and an absent or very small Q, a large R and most constantly of all, an absence of S in lead III Out of these 47 there were only 4 with S III and in these it ranged from 3 to 8 mm in depth The average figures for the size showed that R I, Q III and S III were small, 2 8, 1 7, and 0 4 mm respectively, while S I and R III were large, 12 9 and 13 3 mm respectively

The QRS complexes in lead II may be of the R type (23 cases) or S type (15 cases) or mixed (9 cases) or with very small QRS complexes (4 cases)

Now and again one meets with a case that does not show a high degree of right preponderance Case 6 is an example where there was no preponderance possibly indicating a single ventricle as well as the usual features of Fallot's tetralogy, the result of operation was very successful but the colour was not improved as much as in most cases In Cases 1, 30, and 37, all successful operations, there was less right preponderance than usual Some cases showed a moderate R I in addition, of course, to the very deep S I

T wave abnormalities were uncommon except for T III inversion in 11 cases it was sharply inverted and in 7 it was flat or slightly inverted There were no T II inversion except in Case 30 where it was biphasic

In two, T I was inverted (Cases 42 and 47) and in one it was flat (Case 17) In Case 42 for some unknown reason it became normal and upright again six months later, before his operation In Case 21, T I was enormous, 11 mm in amplitude, and T III was deeply inverted Fairly large T waves in lead II with an amplitude of over 5 mm occurred in 8 cases

As with the P waves, the T waves in some of these cases showed variation in height, unlike most other types of heart disease where the size and shape remain remarkably constant The S–T interval was often elevated in lead I and sometimes became more normal after operation

OPERATIVE EXPERIENCES

In these first 50 cases the original basic technique, as recommended by Blalock, has been closely followed, in 6 other cases valvulotomy was performed or attempted Pott's modification (anastomosis of aorta to pulmonary artery) was not used in this series, although it has been since

The Blalock operation of anastomosis of a systemic artery to a pulmonary artery is always difficult and exacting technically, even when the anatomical conditions are favourable and the anastomosis proceeds smoothly At times, when conditions are not favourable, it becomes an operation of really great difficulty and calls for all the surgeon's technical ability Some of the earlier, more difficult cases were especially exacting, and even with increased experience it is found that a series of straight-forward operations is suddenly interrupted by a complex anatomical situation calling for great patience and not a little endurance

This is not an operation for the casual operator and indeed, quite apart from the pressure of the waiting list, it is desirable that the surgeon should operate regularly In Blalock's clinic one operation a day is aimed at, it has not been possible to achieve this here because routine thoracic work must still be done, but a desirable standard should be two or three operations a week Success is not possible without good team work and one must stress in particular the invaluable part played by the anæsthetists, Rink, Hellwell, and Hutton (1948) have already written a preliminary record of their experiences

Often, these cyanotic patients are not in the state of general health that one would ordinarily demand before embarking upon a severe operation, they may run a low fever, even with sharp rises, or have recurrent or persistent minor upper respiratory infections, etc While it is clearly folly to operate in the presence of considerable pyrexia or recent increase of illness, we have learnt that it is often better not to wait for seemingly ideal conditions, which may in fact never materialize It is sometimes best to seize the opportunity offered, for conditions may deteriorate rather than improve

Moreover, once the anæsthetic or operation has been begun it is desirable, however unfavourable the outlook may appear, to press steadily on until it becomes quite clear that success is impossible This applies not only to anatomical difficulties but to physiological ones as well On several occasions the anæsthetist has reported the patient's condition as very grave and the temptation to abandon the operation has been great In almost all of these cases continuance with the operation after a short wait has been rewarded by final success The most striking example of the soundness of this policy came in the case of a small child (Case 41) aged 5 years, who was extremely ill, she was deeply cyanosed, with severe recurrent pain in the chest even when resting in bed, and was incapable of any activity at all During induction of anæsthesia a bronchial spasm developed and she stopped breathing, and it was only with the greatest difficulty that the anæsthetist could inflate her lungs with an intratracheal tube in place, her heart then also stopped Whether she was then dead is a nice point Intracardiac injection of adrenalin was given and artificial respiration continued The heart started again but spontaneous respiration did not begin for another 40 minutes, her condition was, of course, still desperate At the end of an hour her condition had begun to improve and after much deliberation the operation was started, for it was certain that no second attempt could be made and the outlook was otherwise hopeless The operation was completed and the child made an excellent recovery, ten days later she was learning to walk about the ward, a thing she had not been able to do before She has continued to do well

All our greatest hazards have appeared in the operating theatre, in this series the deaths occurred either in the theatre or within a few hours of return to the ward If the patient left the theatre in even fair condition, recovery always followed There was only one instance of bleeding from the anastomosis, that of a man aged 27, very disabled, very blue, who had already had a hemiplegia, he died several hours later from hæmorrhage from the anastomosis which had been quite dry when the chest was closed (Case 48) Bleeding may, of course, occur temporarily when the clamps are

first undone but it either stops spontaneously or has been controlled by insertion of fresh sutures In one or two of the earlier cases this re-suturing led to narrowing and impairment of the efficiency of the anastomosis and was responsible for some of the poor results

It has been our experience that patients over 20 years of age carry a far greater operative risk, not only are they commonly severely disabled, but their heart muscle seems to have suffered from the long-continued strain, in contrast to the younger children in whom the myocardium seems surprisingly good In addition the anatomical hazards may be greater, and the fatal hæmorrhage in this last case was certainly due to the very thin-walled pulmonary artery, aided by a certain degree of extra strain on the anastomosis during systole as the subclavian artery curved down over the prominent aortic arch

SURGICAL PROBLEMS

Certain general technical features of the operation need discussion in the light of our experiences, for most of these features introduce important practical problems that concern, or should concern, the surgeon undertaking this work

(*a*) *Blalock's operation or the Potts' modification* Although the Potts-Smith modification of aortic-pulmonary anastomosis was not used in this series, it has been employed since and has attracted sufficient attention to make it desirable to discuss its advantages and disadvantages It should be realized that it does not introduce a new principle, but is a technical modification based upon the original principles laid down by Blalock and Taussig They postulated that certain cases of cyanotic congenital heart disease in whom pulmonary stenosis existed could be improved by anastomosing a systemic artery to a pulmonary artery in order to increase the flow of blood to the lungs, and in their preliminary discussions mentioned the use of the aorta as a possibility in place of one of its branches It remained for Potts and his colleagues to introduce the ingenious clamp that made this possible

The advantages of using the aorta would appear to be as follows

(1) The operation may be easier and quicker
(2) It is especially useful in small children in whom the subclavian may be too small to furnish an adequate additional blood-flow to the lungs
(3) It allows the size of the stoma to be varied at will and to be measured exactly
(4) It may provide a ready solution to the problem of the case with a difficult, deep, short, and narrow subclavian artery
(5) It avoids the dangers of cerebral damage

associated with the use of the carotid or innominate arteries
(6) It is the simplest, and sometimes the only, way of overcoming the problem of a very high aortic arch with its branches arising at the very root of the neck (Fig 7)

The disadvantages of using the aorta would seem to be as follows

(1) It demands a postero-lateral approach (the operation is probably possible, but certainly very awkward through an anterior incision)
(2) It may be very difficult if the aorta is right-sided, as occurs in about one quarter of the cases This is because the right pulmonary artery is often very short and deeply placed in the mediastinum
(3) The pulmonary artery may be so small and narrow that it cannot be used, whereas a small thin artery can still sometimes be employed efficiently for end-to-end anastomosis with the subclavian
(4) In older patients there may be too much disproportion between the size and thickness of the walls of the pulmonary artery and that of the aorta to make a safe junction
(5) Direct aortic-pulmonary anastomosis may cause a greater strain on the heart and a greater risk of pulmonary œdema

It is still too early to make a final assessment of the Potts' modification, but the most certain advantages it offers would appear to be a more rapid and less elaborate dissection when the aortic branches are small and deeply placed in the mediastinum, or arise very high in the chest, the possibility of adjusting the size of the stoma to meet the needs of the individual case, especially in very small children, and freedom from the dangers of cerebral damage following use of the carotid or innominate arteries

In cases where it would be about as easy and satisfactory to use either the subclavian artery or the aorta, it would seem to be surgically sounder and wiser to use the subclavian and to avoid exposing the patient to the greater perils that must attend the deliberate manipulation of a structure of such importance as the aorta After all, if some mishap befalls the subclavian artery the situation can readily be remedied by ligating it and the aorta could then be used If some mishap occurs when the aorta is being used it would certainly be more difficult, and perhaps impossible, to retrieve the situation

(*b*) *Antero-lateral or postero-lateral approach* Blalock's practice of using the antero-lateral intercostal incision was followed almost exclusively in the first 50 cases, but has often been departed from since then The antero-lateral thoracotomy incision

Fig 7 —Case PO35   Angiocardiogram at 3 seconds   This shows a left-sided aorta which is dilated and very high, with the innominate rising in the ridge of the neck to the right where it had been easily felt in the neck   The illustration also demonstrates the large right to left shunt with pulmonary stenosis

has always been more popular in American surgery than in that of other countries, as witness the popularity enjoyed by the anterior approach for pneumonectomy and for ligation of the patent ductus arteriosus   In a very ill patient the antero-lateral approach may throw a smaller strain on the lungs and circulation than a postero-lateral one In general, however, the exposure provided by the antero-lateral intercostal incision may be very cramped, and if the ribs are awkwardly shaped so as to make a high narrow chest, the difficulties of dissection and ligation of the highest branches of the subclavian artery may be extreme   In such cases the faulty exposure commits one to a set of circumstances that really constitute faulty surgery

One important reason that determined the use of the antero-lateral approach in many cases in this series was our policy of opening the pericardium and examining the heart condition carefully to make as complete a diagnosis as possible and to be prepared to perform a valvulotomy if indicated The pericardium can, of course, be opened and the heart inspected through a postero-lateral incision,

but it would be difficult to utilize the right ventricular approach to the pulmonary valve without consider able and most undesirable dislocation of the heart

Our present practice is to use the antero-lateral approach only in those cases in which it may be necessary to operate directly upon the right ventricle itself   For all other cases a postero-lateral incision is used with resection of the whole length of the fourth rib from transverse process to costal cartilage The resection of the rib is much more satisfactory than an intercostal incision which causes more bleeding at the time and may cause dangerous or even fatal oozing afterwards, the risk of bleeding is increased by the use of pericostal sutures which are also a cause of unnecessarily severe post operative pain   The postero lateral thoracotomy with resection of a rib is followed by far less pain than either a postero-lateral or antero-lateral intercostal thoracotomy   The exposure afforded by the long postero-lateral approach is a great advantage and allows a much more easy, rapid and safer exposure of the vessels and inspires the surgeon with much greater confidence that he has

more complete control of the situation. There is no difficulty in application of the pulmonary artery clamp provided the incision is carried well forwards, the performance of the actual anastomosis is easier than from the front. Moreover, the postero-lateral incision allows use of either the subclavian artery (Blalock's operation) or the aorta (Potts' modification), according to the conditions found

With but few exceptions, in which the third intercostal space was used, all the operations by the antero-lateral route have been done through the second interspace which is definitely preferable except in very small children

(c) *Right or left side*. Blalock's earlier recommendation was to use the side opposite to the aortic arch in all but adults and patients in the later teens His reasons for this were that if the subclavian is used as it arises from the innominate it forms a more satisfactory angle with the parent vessel when it is turned down for the anastomosis whereas if the subclavian is used as it comes off the aorta it may be sharply kinked at its origin, or flattened as it passes over the prominence of the aortic arch Also, if the subclavian artery is found to be unsuitable the innominate or the carotid artery can be used instead

In his latest paper Blalock (1948b) states that he uses the right side (when the aorta is left-sided) in all patients between the ages of 2 and 12, but prefers the left approach in children below 2 and in patients over 12 who have attained most of their growth or who are more than 5 feet in height. He mentions that some other surgeons have preferred to use the left-sided approach for all cases

Blalock's earlier recommendation was followed in most cases in this series, but, recently, departures have been made. In spite of increasing familiarity and experience with the operation the dissection of the systemic arteries on the right side may be extremely difficult, not a little dangerous, and certainly very exacting, especially so when the superior vena cava is large and dilated. It was therefore decided to extend the use of the left-sided approach to children under 12 years as well as to older patients and this was done successfully in a number of cases and with much greater ease, even though the subclavian may appear unduly kinked and flattened at the time the result has been just as good, and it seems probable that the artery elongates and adapts itself. The right-sided approach was then used again on a small child aged 5 years (Case P043) and after a long, tedious, and exacting dissection a very deeply placed and long innominate artery was found which divided high up near the superior thoracic inlet and gave rise to a

subclavian artery too short to bring down to meet the right pulmonary artery. This could have been done if the carotid artery had been ligated and divided but in addition to the carotid another artery almost as large passed into the neck and it seemed that the two vessels must carry a large supply of blood to the head and brain. Alternatively the innominate could have been used, but in addition to the dangers of cerebral ischaemia this artery was so large that there seemed considerable danger of causing heart failure and acute pulmonary œdema if it were used. Accordingly the operation was abandoned with the idea of using a left-sided approach on a later occasion. This experience has finally decided us in favour of using the left-sided approach in all cases unless angiocardiograms suggest the right pulmonary artery is small or absent, indicating it would be dangerous to occlude the left branch while the anastomosis is made. The only other indication for a right-sided approach is the presence of a right aortic arch in a case on which one wishes to do the Potts operation

(d) *The use of the carotid or innominate arteries* The danger of cerebral ischaemia is very real if the innominate or carotid arteries are used, in Blalock's series the mortality was 30 per cent. The carotid was divided to allow the innominate to be turned down in two patients in this series (Cases 24 and 35) and in one since (Case P034). The first did extremely well, the second developed an acute pulmonary œdema as soon as clamps were removed and the anastomosis allowed to function, and died after a few hours, the third became comatose and hemiplegic soon after operation and died the next day. Blalock (1948b) in his last paper emphasizes that the carotid or innominate should not be used if it can be avoided and states that in many of his earlier cases in which one of them was used, a little longer careful and patient dissection of the subclavian might have spared the carotid or innominate. It would appear to be purely a matter of chance whether interruption of the carotid circulation is followed by paralysis or death or by a good result. It is indeed a gamble, and a poor gamble as well, and therefore is neither surgically nor morally sound. In our opinion, the use of the carotid or innominate arteries is unjustifiable and should be abandoned

If the surgeon is contemplating using the right-sided approach he should first of all study good angiocardiograms which display the disposition of the aortic arch and its branches. In this way he should be able to assess whether or not it is likely to be possible to use the right subclavian artery This is a far better way in which to obtain the information than a thoracotomy. An unfavourable

arrangement of the great vessels, such as would make sacrifice of the carotid blood-supply inevitable, is seen in Fig 7, 8, and 9   In Fig 7 the aortic arch is unusually high and the innominate artery actually lies above the clavicle and could be seen and felt in the neck, clearly Blalock's operation would be impossible on either side without using a long length of carotid artery from the neck   Such an arrangement seems to demand Potts' operation, which was successfully used in this case   In Fig 8 and 9 the position of the innominate artery, deep in the mediastinum, is clearly seen and also its very high division with a resultant very short subclavian artery   In these cases the left subclavian artery was successfully used for the anastomosis

(e) *Absent or small pulmonary arteries*   The value of angiocardiography to display the disposition of the aorta and its branches is clearly proven in these cases and it has been of equal value in others   It has been less satisfactory in displaying the main pulmonary artery and its right and left branches, often because of the slow and feeble concentration of the opaque solution in them due to pulmonary stenosis, and especially when a large and rapid shunt has caused the contrast medium to pass rapidly into the systemic circulation   In the normal patient it may be easier to display the chief pulmonary arteries more clearly, especially when oblique or lateral views are used in addition to the postero-anterior ones   One must be prepared to be disappointed with the delineation provided when pulmonary stenosis exists with a large shunt

The angiocardiograms may, however, indicate that one pulmonary artery is either entirely absent or very small   Fig 10 shows an example in which the left pulmonary supply seems much smaller than the right   This suggests that it would be unsafe to use the right pulmonary artery as death would probably soon follow its necessary occlusion while the anastomosis is being made   The demonstration or suspicion of a small right pulmonary artery would provide an indication for using a right sided

FIG 8 —Case C017   Angiocardiogram at 3 seconds, showing the origin of the innominate artery fairly deep in the mediastinum with a high division of the subclavian from the innominate and a large gap that would have had to be bridged between this and the pulmonary artery   It also shows an over-riding aorta, a high grade of pulmonary stenosis, and a dilated superior vena cava
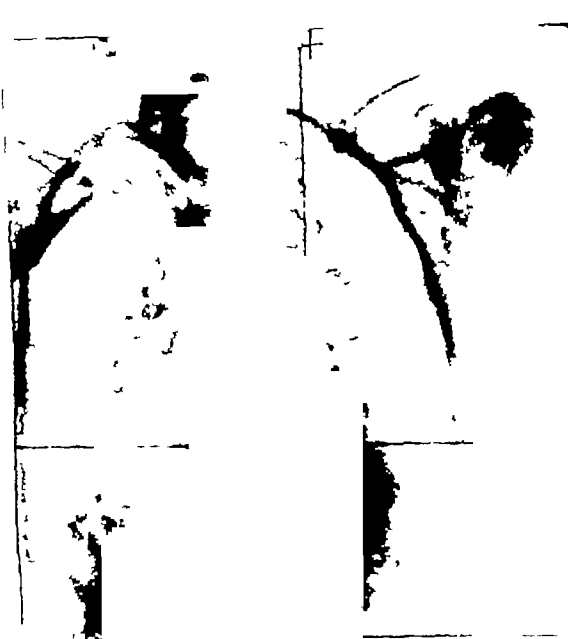
FIG 9 —Case 0053 Angiocardiogram at 3 seconds It shows the origin of the innominate artery fairly deep in the mediastinum with a high division and a resultant short subclavian artery that would have been difficult for a pulmonary anastomosis It also shows an over-riding aorta with moderate pulmonary stenosis

FIG 10 —Case P048 Angiocardiogram at 4 seconds which suggests that the left pulmonary artery provides a much smaller blood supply than the right and that it would probably be unsafe to occlude the right branch Operation will, therefore, be performed on the left side

approach in preference to a left-sided one   Careful screening and plain radiography may also enable one to identify both pulmonary arteries or to suspect that one is small or absent

In one case, after a long dissection, the right pulmonary artery was found to be not much larger than an intercostal artery and so could not be used, no ill-effects followed the exploration (Case 27) In another (Case 17) the right pulmonary artery was prepared and had been clamped for 12 minutes when the heart stopped, it was assumed that this was due to absence or obliteration of the left pulmonary artery   The heart was started again after massage and injection of adrenalin, and end-to-end anastomosis was performed between the subclavian artery and the first branch to the right upper lobe   Unfortunately the heart stopped several times and finally could not be started again, autopsy confirmed that the left pulmonary artery was completely obliterated   Such cases sometimes are unavoidable and part of the hazards of the procedure, but may be avoided by more careful radioscopy of the pulmonary arteries

(*f*) *End-to end anastomosis*   In order to secure extra length of vessels Blalock not infrequently ligates the pulmonary artery medially, divides it, and performs end-to-end anastomosis to the subclavian   This can be a most valuable step in some of the more difficult cases and may indeed be the only possible way to bridge a gap when the subclavian is short   It is especially useful when, on the left side, the prominence of the aortic arch threatens to kink and flatten the down-turned subclavian artery and to cause tension on the anastomosis It should certainly be used in preference to end-to-side anastomosis to a narrow pulmonary artery in which most of the width of the pulmonary artery would be encroached upon by the anastomosis One is naturally reluctant to take the step of ligating and dividing the pulmonary artery but, as Blalock says, a good end-to-end anastomosis is always preferable to an uncertain end-to-side one   The only difficulty may arise from considerable disproportion between the two vessels, Blalock states that he does not mind this provided the pulmonary artery is no more than two to three times the size of the subclavian

Potts' modification may provide an easy alternative if the subclavian artery is too short to use without end-to-end anastomosis, but if the main

difficulty lies with a small and narrow pulmonary artery, aortic-pulmonary anastomosis may be difficult or impossible and direct end-to-end anastomosis with the subclavian is much the safer and better

End-to end anastomosis has been used twice in this series (Cases 8 and 17) and has been used twice since

SUMMARY OF SURGICAL PROCEDURE

We believe, in the present state of our experience, that the most useful and most satisfactory incision is a left postero-lateral one with resection of the whole length of the fourth rib and incision of the rib bed This gives a perfect exposure, enabling rapid, comfortable, and much safer dissection of the vessels and also permits use of either the subclavian or the aorta for the anastomosis We reserve the antero-lateral approach for those cases in which we anticipate that right ventricular cardiotomy may be needed for valvulotomy

We have abandoned the right-sided approach except for cases in which radioscopy and radiography (including angiocardiography) suggest the right pulmonary artery is unduly small or absent A right-sided postero-lateral incision is needed if Potts' operation is contemplated in the presence of a right aortic arch

In general we use Blalock's operation in preference to Potts' modification when it is feasible The greatest value of Potts' operation is in small children in whom the subclavian artery is too small to furnish an adequate extra flow of blood to the lungs, and in older patients when the subclavian artery is too small or too short and it would otherwise be necessary to use the carotid or innominate arteries We feel the use of either of these vessels is unjustified, owing to the much higher mortality from cerebral complications or cardiac failure and to the risk of permanent residual paralysis End-to-end anastomosis of the pulmonary artery and the subclavian artery has a useful place when an end-to-side anastomosis would be difficult, impossible, or under undue tension

Angiocardiography is an invaluable method to allow pre-operative study and assessment of the pulmonary and systemic arterial pattern

Much emphasis has been laid on the difficulties and anxieties of these operations but this gloomy side is relieved by the more satisfactory side of success In spite of the hazards and long hours of work one derives great satisfaction from contemplation of the successfully completed anastomosis and the rapid, indeed at times dramatic, improvement that follows the operation As stated elsewhere an excellent result was obtained in 66 per cent, a most gratifying figure when one considers the very poor material with which one is working

POST-OPERATIVE TREATMENT

In our experience the post-operative period is much less stormy and anxious than might be expected Children particularly tolerate the extensive and prolonged thoracic exploration remarkably well, and the difficulties encountered have been mainly in the older subjects Penicillin therapy is started 24 hours before operation, and pre-operative instruction in breathing exercises is a routine Cyanosed and polycythaemic patients should never be left for long periods without fluids and particular care should be given to the fluid intake before operation as a simple precaution against the additional danger of thrombosis at this time

These patients are well fortified against blood loss during the operation so that transfusion of blood is not needed during or after the operation, but plasma or gum saline are given to combat shock, and the drip is continued on return to the ward They are encouraged to drink as soon as they recover consciousness The need for intravenous fluids seldom continues longer than 24 hours, unless the blood pressure fails to rise—it is usually back to the pre-operative level or above in 12 hours—or unless cerebral thrombosis is a complication An adequate fluid intake of at least 1000 ml in a small child to 2000 ml in an adult is needed to prevent thrombosis in the days after operation, and is best given by mouth With increasing experience we have found that the amount that has had to be given intravenously has decreased, in the first 15 cases it averaged 37 ounces while in subsequent cases it has dropped to an average of 25 ounces Blood transfusion was needed only in two cases, in one (Case 5) who bled into the pleura and in one (Case 8) who had profound postoperative shock

The patient is nursed in an oxygen tent on return to the ward and the time that this is needed is judged by tentative periods of removal without development of cyanosis or distress The time varied from six hours to four days, with an average of 36 hours Any delay in regaining consciousness or inability to move a limb must be noted as an indication of cerebral thrombosis Breathing exercises and postural coughing are started as soon as the patient is conscious and it must be emphasized that though this may seem unkind, almost brutal, after a serious operation, the children are not unduly disturbed and insistence on this early stimulation is amply repaid by the rarity of serious chest complications A portable radiograph is taken within the first 24 hours and at frequent intervals subsequently for evidence of collapse and particularly for pleural

effusion Our experience is that morphine should be used with great care, it is not always needed in the first day, and seldom afterwards In those with distress from coughing, and this is not common, codeine is useful

There is an immediate rise of temperature after operation but very seldom above 101°, and excluding four cases with complications where it was prolonged over ten days, the average duration was five days The pulse rate was the better indication of the general condition it was frequently at its highest in the second 24 hours, and had usually settled to a steady level of 10 points above the pre-operative level by the end of the first week The close correlation between temperature and pulse rate, particularly the latter, and the presence of a pleural effusion is mentioned later

Two indications of the degree of success of the anastomosis in the period immediately after operation are the colour, and the presence of a murmur There is an immediate improvement in colour at operation as soon as the anastomotic circulation starts, but at this time controlled respiration is occurring In a successful case this improvement in colour is maintained in the oxygen tent, and after a short period of up to 48 hours will continue outside it Some cyanosis must be expected from the right to left shunt which remains, and this will be increased if breathing is embarrassed by obstructive secretions in the respiratory tract or by pleural effusions If these factors are taken into account, a comparison of the colour after operation, particularly of the extremities, with the depth of cyanosis before operation is a reliable guide to the degree of functional improvement that may be expected

The thrill over the anastomosis, which can be felt by the surgeon, is followed after operation by a murmur heard with the stethoscope, this is usually continuous as heard over a patent ductus arteriosus but may be systolic and diastolic or merely systolic Though chest complications may make recognition more difficult in the first few days, its presence is an encouraging sign of success and its absence suggests that thrombosis has occurred at the suture line and that the anastomosis is not patent We have become increasingly impressed with the murmur as a sign that a good result may be expected when the patient is able to start walking, which is usually after the first week

There are three important post-operative complications cardiac failure, which is rare, pleural effusion, which is common but generally harmless, and cerebral thrombosis, which is the gravest

One of the criteria for operation is a heart that can adjust itself to the altered circulation which the anastomosis causes, so that much enlargement of the heart is a contraindication In this respect the selection of cases would appear to have been satisfactory for there have been few difficulties or anxieties on account of the heart The blood pressure rises to the pre-operative level, or above, in the first 12 to 24 hours, and any delay in this rise favours the development of thrombosis and calls for the exhibition of a " pressor " drug, such as methedrine, and plasma transfusion This happened in one of our early cases (Case 8), an adult, where the pressure fell to 50/40 and the systolic was below 100 for the first 36 hours, he developed a cerebellar thrombosis in the first 24 hours A rise well above the pre-operative level is mentioned by Taussig but we have not experienced it, should it occur, a venesection would be indicated

It might be expected that the sudden increase in the pulmonary circulation, with the additional work demanded of the left ventricle by the anastomotic shunt induced by the operation, might cause pulmonary œdema in the early post-operative period We have not experienced this in any case surviving operation though it occurred in one death after operation (Case 35) in one lung on the side where the innominate had been joined to the pulmonary artery Case 21, a poor result as judged by colour and the absence of a murmur over the site of anastomosis, was slow to recover from this operation, and, despite the absence of a pleural effusion, his temperature failed to settle till the 15th day On the 27th day he complained of pain over the heart and in the left arm, and was collapsed with ashen cyanosis and dyspnœa, the pulse rose to 140 and the blood pressure dropped to 65 systolic He recovered with morphia but the attack was repeated next day, and again responded to the same drug There was no change in the electrocardiograph to suggest a coronary thrombosis There seems little doubt that these were attacks of left ventricular failure and they were treated as such, he subsequently developed a cerebral abscess which was successfully treated by operation There were no cardiac incidents in the other patients Congestive failure was never seen, nor was digitalis used, despite the increased work demanded by the anastomosis, as shown by the increase of heart size after operation in most cases

The second complication of pleural effusion on the side of the operation is common and occurred in 32 of 43 cases after operation, in 11 it was of moderate size but in 21 it was large enough to demand aspiration, and in 10 of these, more than once The fluid commonly developed immediately after operation, or in the first few days and naturally it is usually blood-stained An average example

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is shown in Fig 11 But effusion may suddenly increase, recur, or even first develop later in convalescence and this happened in 5 cases An early effusion successfully aspirated is on the whole less of a handicap in convalescence than the slowly developing effusion where aspiration is hardly necessary in the first few days and the decision is delayed It is in these cases that later and repeated tappings are necessary, often difficult, and incomplete in their results It is these patients particularly whose stay in hospital is prolonged, whose temperature and pulse fail to settle, and 5 such cases were discharged with " pleural thickening " on radiography or showed a very small residual effusion all cleared up subsequently

The temperature and pulse chart reflect remarkably clearly the presence of fluid in the chest, an early effusion successfully aspirated is associated with a quick return to normal temperature and pulse rate a rise on the second and third day, which is not uncommon, almost denotes a slowly developing effusion a sustained temperature and pulse indicates the persistent effusion, so hampering in convalescence while with one exception—the case with left ventricular failure—a rise in pulse later in convalescence always pointed to the pleura as the cause This last point was well shown in Case 39 whose convalescence was extremely satisfactory until the 19th day when he complained of abdominal pain and felt unwell, a rise in pulse rate was the only significant sign but it was sufficient to predict that an effusion was developing on the operative side It was apparent to clinical signs and radiography the following day and aspiration allowed his convalescence to continue uninterrupted The late effusion was best illustrated by Case 2 who had a small effusion late in convalescence which resolved, but after returning home a massive effusion developed and necessitated readmission to hospital (Fig 15, Campbell, 1948) We have regarded these as mechanical setbacks and have not allowed them to retard progress by prolonging bed rest unduly, and this, with the exception of Case 2, has been justified for subsequent examinations have shown a clear and moving diaphragm There has been no evidence that these effusions are associated with pulmonary emboli and, except once where a very small amount of fluid was noted on the opposite side, the effusions have always been on the side of operation Persistent haemorrhagic effusion occurred in Case 5 only, necessitating transfusion, repeated aspiration of 11 pints in all was needed over 4 weeks, the fluid gradually decreasing in colour and gradually in amount until it quite suddenly stopped and did not recur The correlation between temperature and effusion is roughly shown

by an average length of 3 days in those with no fluid, of 5 days in those with moderate effusions, and of 8 days in those where aspiration was needed

The third and most serious complication of cerebral thrombosis occurred in 3 of the 43 post operative cases Case 1, a boy aged 7, with a haemoglobin of 126 per cent, had a history of a brain abscess on the left side when 2 years old A right hemiplegia of moderate severity which was noted immediately after operation began to improve on the seventh day and when he was discharged on the sixteenth day there was only a slight limp He has made a complete recovery Case 8, an adult, was a severe case with haemoglobin of 141 per cent and had the severe drop in blood pressure in the first 36 hours already noted The two factors of marked polycythaemia and shock were therefore present to encourage thrombosis, and this was noticed in the first 24 hours, the left anterior cerebellar artery being involved Recovery from this was complete but on the eighth and twenth fourth days he had thrombosis of systemic arteries and on the twentieth day a thrombosis of the anterior cerebral artery From this severe complication he has made a gradual but not a complete recovery, a disappointment in view of the excellent physical result The third, Case 29, was a boy of ten, with a haemoglobin of 158 per cent, he was drowsy after operation and was found to have a thrombosis of the cortical ascending parietal branch of the left middle cerebral affecting the arm area. The blood pressure was not unduly low after operation but during the operation there was marked collapse when the right pulmonary artery was occluded, and it was probably then that the thrombosis occurred He is left with impairment of movements of the right arm and hand, a considerable disadvantage though compensated by an otherwise excellent result

A further severe complication which we regard as due to the operation was in Case 21 who was admitted to Oldchurch County Hospital one month after discharge from Guy's after a prolonged post operative stay of 56 days due to persistent temperature and left ventricular failure as already mentioned The cause of this was a cerebral abscess which was successfully dealt with by aspiration one month later It is not impossible that a post operative thrombosis was the basis of this complication, though it was some time after

It will be seen that cerebral thrombosis is the most important complication and one which to a lesser or greater degree nullifies the physical benefits that an otherwise successful operation gives It should be most feared in those with gross polycythaemia
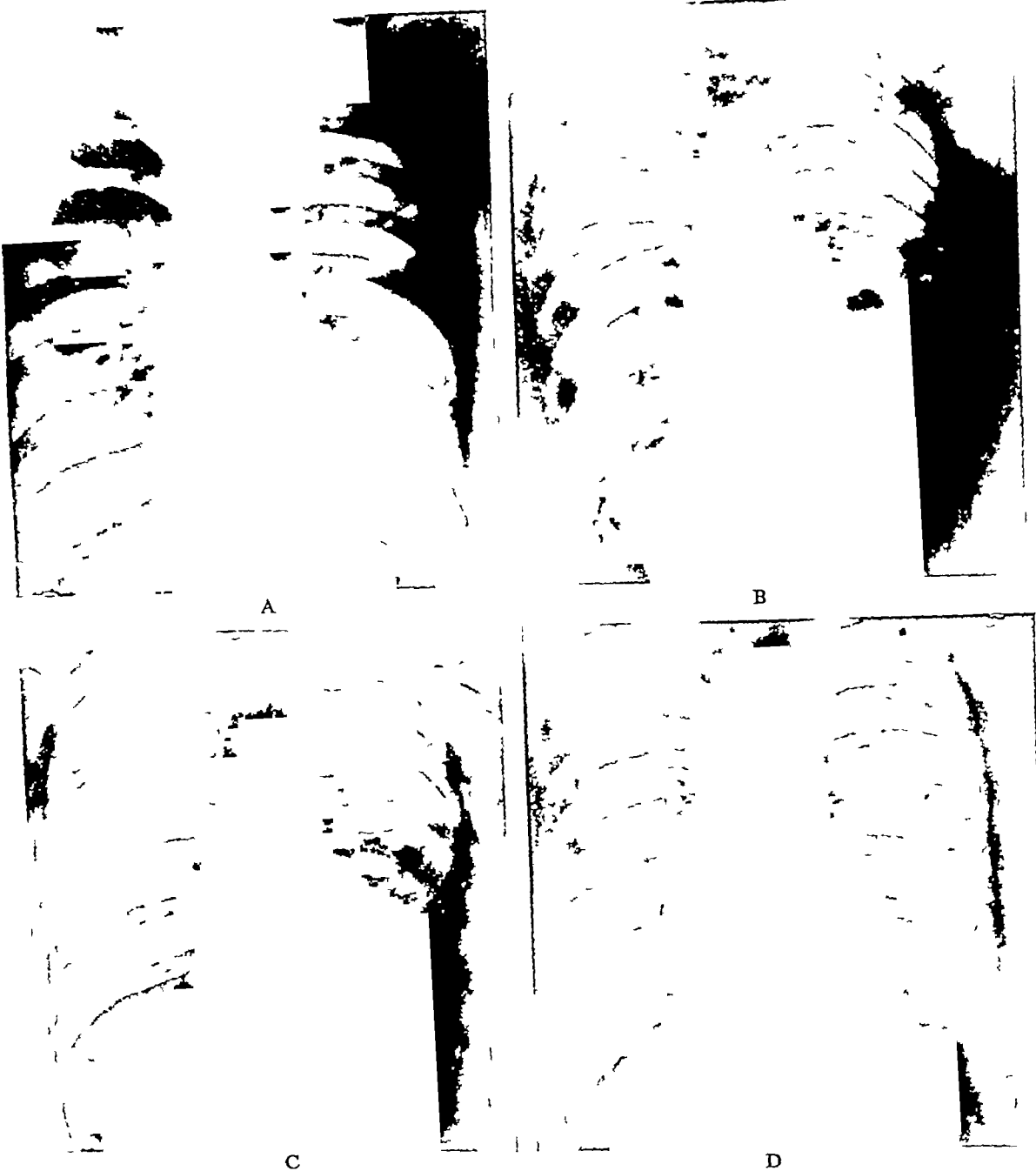
FIG 11 —Case 26 (Reference No P069)

(A) Teleradiogram in P A position before operation showing the clear lungs and some pulmonary bay with a raised apex   Both pulmonary branches can be seen (9/1/48)

(B) Portable radiogram one day after operation, showing a moderate sized effusion at the left base with some collapse (11/2/48)

(C) Portable radiogram showing gradual clearing of the effusion, the heart size becoming more visible but not yet easy to measure accurately

(D) Teleradiogram, 7 months after operation, showing some increase in heart size from before operation, c t r 54 instead of 46 with less apparent change in the density of the lung than in many cases, although the result was most successful

with severe operative and post-operative shock, and in adults more than children   Prophylaxis with anti-coagulants introduces the danger of hæmorrhage and for this reason we do not use it   Nor have we felt sufficiently confident to start treatment by heparin within three days of operation, though there is a strong case for giving it promptly if thrombosis is diagnosed   If blood loss at operation has not been great, and polycythæmia is still present, blood letting is indicated and also intravenous fluids, by which method the heparin can be given

In comparison with these three, other post-operative complications are slight   Some collapse of the lung on the side of operation, independent of effusion, occurred and required no treatment except continuation and insistence on breathing exercises   A small pneumothorax was present in one case and required no treatment and in only one was surgical emphysema of any degree present   Obstruction to breathing by secretions in the upper respiratory tract is largely obviated by insistence on breathing exercises and postural coughing, but was present in 17, though in only 4 did it cause any anxiety   Case 3 responded to the old fashioned steam tent, and Case 49, after 36 hours of obstructed breathing, to the more old fashioned method of turning him upside down, both exhibited by a watchful and wise ward-sister   Cases 40 and 41 both had severe laryngitis, and in the first, where a heavy growth of yeasts was cultivated from a throat swab, tracheotomy was necessary but led to little delay in his complete recovery

The disability in the arm on the operated side is remarkably slight, and though the vascular change is apparent in signs, symptoms are slight and the disinclination to move it is soon overcome   A diminution in the size of the pupil on the side of operation, occasionally with ptosis, is almost a constant finding but had generally disappeared by the time the patient was discharged   No disturbance in kidney function was noted

On the whole the postoperative period is surprisingly tranquil and uneventful for such an extensive and eventful operation   Children stand it particularly well and it is the adolescent or adult who is more likely to present difficulty   No better example of this can be shown than Case 41, a gravely ill girl of 5, whose heart, as well as breathing, stopped during induction of anæsthesia   Despite this and an operation lasting over three hours, and later a severe tracheitis, she was out of bed on the fourth day   Excluding 12 cases where the stay was prolonged on account of cerebral thrombosis, wound sepsis, or pleural effusion, the average stay in hospital was 23 days, and the average time in bed was only 7 days

RESULTS OF OPERATION

In these first 50 patients there have been 7 deaths, a mortality of 14 per cent   Two of these deaths were among the relatively small number of patients of 19 and over (Cases 1A and 48)   One had a single pulmonary artery and died when it was clamped (Case 17)   In the others, there seemed no special reason except their serious condition and the severity of the operation (Cases 12, 32, 35, and 38)

Fallot's tetralogy was present in five of the seven   The remaining two had somewhat more complicated forms of morbus cœruleus, one having a single auricle in addition (Case 35) and the other having an infundibular stenosis, an aorta arising from the right ventricle without transposition of the pulmonary artery, and a small left ventricle with its only exit a ventricular septal defect (Case 32)

There were three patients where no anastomosis could be performed   One, an error in diagnosis already described, because the pressure was high in the pulmonary artery (Case 28), one because the right pulmonary artery was too small (Case 27), and one because of the technical difficulties introduced by the enormous dilatation of the collateral circulation (Case 14)   In no case was it impossible to find a suitable systemic artery, but often the shortness of the subclavian led to practical difficulties and was, we think, sometimes the reason for the lack of success   This leaves 40 cases to be considered

There were three where, in our opinion, there was no improvement (Cases 11, 19, and 22), though even then the parents of two thought there had been some   In one, the anastomosis was thought to be too small at the time (Case 11) and in a second there was bleeding from the anastomosis when it was nearly completed, and to save the patient's life many stitches had to be put in that probably led to some intra-arterial thrombosis and occlusion of the anastomosis (Case 22)   It is possible that these three were also errors in diagnosis and not technical failures of the operation, but we do not think so

In four the result has only been included as "fair"   In one of these a similar difficulty with bleeding from the anastomosis occurred (Case 43), after operation he was able to walk upstairs which he had never done before but was not greatly improved   In the second (Case 21) the result was at first classed as a failure and after a long convalescence a cerebral abscess followed   when seen later after this had been cured, he was certainly improved but not as much as most of the others   In the other two the result was as good as possible as far as the heart was concerned, but the patients were handicapped by thrombosis resulting in partial hemiplegia, in one of these severely (Case 8), and

in the other, causing much limitation of his arm and hand movements but not preventing a great increase in his physical activity, so that he could walk about the greater part of the day (Case 29)

This leaves 33 of the 50 cases (66 per cent) where the result was almost perfect. The patients' capacity was enormously increased up to walking several miles instead of a few hundred yards, or getting about all day instead of being an invalid mainly in the house. To the parents the improvement seemed almost miraculous. One boy (Case 1) who had been tied to his mother's apron strings was at school within two months and after a year was running about all day, playing cricket, and could easily walk 4 miles. After running fast for 25 yards there was slight cyanosis in his lips and nails and some dyspnœa, but this cleared up very rapidly.

Another (Case 2) who had rarely been out of his parents' sight had within a year walked 6 miles and climbed hills in Switzerland as easily as his parents; he was anxious to become a medical student and was doing well at school

Another (Case 4), who had been carried into hospital by his father, was leading a normal life at school and was able to go roller skating within a few months. Case 23, aged 19, who had been a complete invalid, had been on a camping holiday and had walked 6 miles. Such accounts could be repeated for nearly all the patients and all who have done less well have been mentioned individually

The cyanosis was also much improved. In most of them it was absent on casual inspection though it could generally be seen in the nails at rest (but often not in the lips) and tended to be noticeable only on a cold day or after vigorous exertion. In one of the severe cases (Case 6) the cyanosis was still moderate, but it had been extreme and the child was able to do so much more that we feel it right to include her in this group. Case 49, with tricuspid atresia, who was very severely limited has not yet made as much progress as the others, but after leaving hospital fit and apyrexial, he was admitted elsewhere a month later with suspected bacterial endocarditis. He made a good recovery and can get about all day and his limitations seem more his unusually poor muscles than his heart. His colour has improved, but cyanosis can still be seen in his lips. We hope on the analogy of other cases that his improvement will go still further as his muscles improve

The clubbing of the fingers also disappeared in some patients in the course of four or five months, some improvement was generally noticed very early. Where the clubbing was gross it seems more doubtful if it will disappear entirely, though it has changed greatly and become much less noticeable in the course of six months. No trouble has been experienced from the arm where the subclavian was divided, though the brachial pulse has not returned with sufficient strength to be able to measure the diastolic blood pressure in this arm

In nearly all the successful cases a continuous murmur, such as is heard with a patent ductus, has persisted though often the thrill seems less than might be expected with the murmur. This is a good guide to the success of the operation and unless such a murmur can be heard early and easily, it is unlikely that the patient is going to be one of the most successful results. Occasionally, when there was less improvement than usual, there was a systolic murmur only

The enormously increased ability of these patients to get about often reveals orthopædic disabilities that have not mattered previously. Owing to the poor development of the muscles through lack of use and the small blood supply, and sometimes to an added deformity of the limbs from their continuous squatting, their new activity reveals many postural defects. We have made it almost a routine for the patient to have exercises and to be trained in walking correctly, and with simple supervision on these lines and occasionally with wedging of the shoes they have made rapid progress and had no serious difficulties

We were at first a little surprised that there was not a quicker increase in the weight. As already stated, parents were nearly always anxious about the difficulty of making their children eat, and generally the appetite improves at once and they eat well. Probably the greatly increased activity prevents them having anything to spare for putting on weight for a time, but they can be expected to gain after a few months rather than a few weeks, and most of them have increased and gone some way to catch up with the weight that is normal for their age

INCREASE IN SIZE OF THE HEART

One of the points that has been emphasized as a drawback to the Blalock-Taussig operation is the increase in the size of the heart that may be expected from the work added by the left to right shunt. We have, therefore, paid special attention to the size of the heart before and after operation

Of the 50 cases, 7 died, 3 had no anastomosis, and in 3 the operation was thought to have been unsuccessful. This leaves 37 where the heart size can be compared before and after a successful anastomosis. Owing to many of these patients living so far from London it has not been easy to get a regular follow up. We have, however, seen and obtained reasonably comparable radiograms in all

A   B
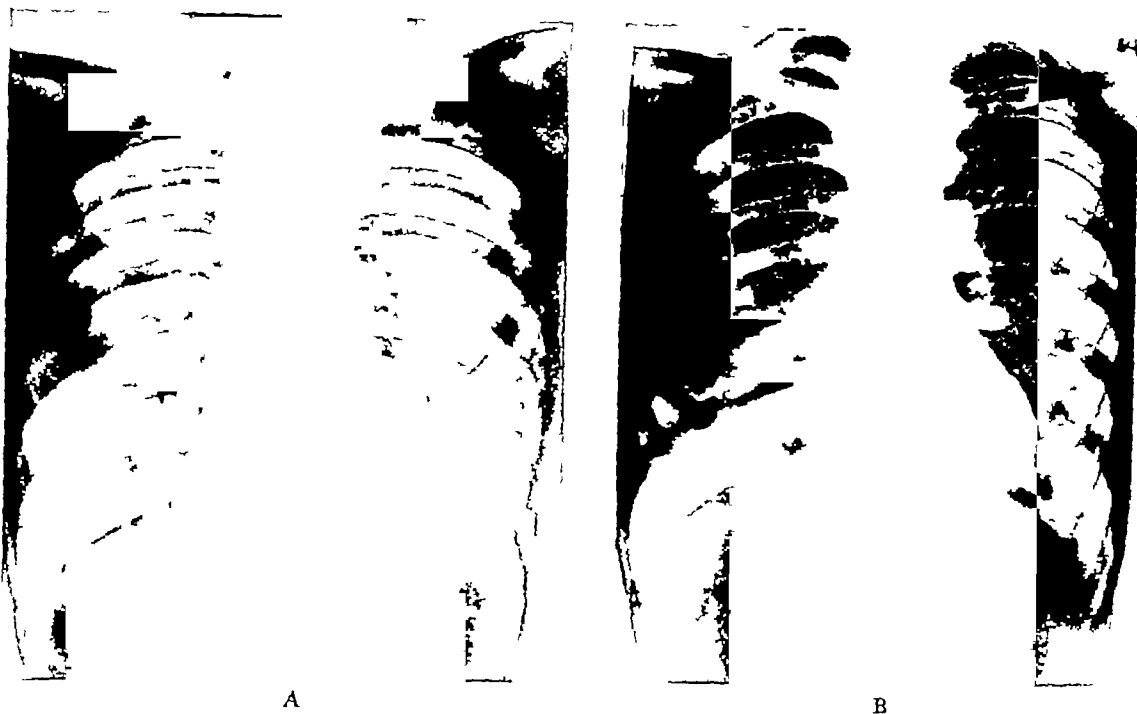
FIG 12 —Case 23 a boy aged 19, with Fallot s tetralogy

(A) Before operation, showing a slightly raised apex and a straight left border

(B) Eight months after operation showing some increase in the size of the heart, the c t r being 48 instead of 42, but still within normal limits   There is also some increase in the shadow of the pulmonary artery, especially on the left, the side of the operation as the aortic arch was right-sided

but two where we are relying on reports from their doctors   in neither of these had the heart increased in size a few weeks after operation   In one patient who lived in Cyprus we were fortunate in getting a report and teleradiogram from Dr Hills who had taken the films at Guy's Hospital before operation Examples of an increase of average amount, of very little change, and of the greatest increase we have seen are given in Fig 12, 13, and 14 respectively

This leaves 35 cases to be considered and we have taken separately those where the follow up was more than a year after the operation

Of the cases operated on more than a year ago all 13 have been followed up and teleradiograms have been obtained   Two of these showed no significant change in the size of the heart, but there was some increase in the other 11   In 6 cases there was no further increase after the first month and in another 3 there was little or no increase after about four months, but 2 who had not shown much increase in the first few months showed some increase between four months and a year   The

average increases, shown in Table III might look like a slow but progressive rise, however, consideration of the individual cases shows only 3 out of 13 with any increase after four months (from 51 to 55) Naturally these three will be followed up with special interest to see if they are in fact exceptions

Of the remaining 22 cases, some had been followed up for 11 months and all for more than 7 months, except three so far only followed for 5 months Three of these showed no significant change in the size of the heart, but there was some increase in the other 19   In 10 cases there was no further increase after the first 4 to 6 weeks, in 9 there was some increase after this, but in 4 of the 9 it was only by 2 or 3 points per cent and in another 3 by only 4 points per cent   We had not as a rule, intermediate records at about 4 months in these patients but in the three where we had, the increase had all taken place by this time   The average increases are shown in Table III

Taking the two groups of cases together the average increase in cardio-thoracic ratio was from 48 0 to 52 7 per cent   It had not increased in 5 of
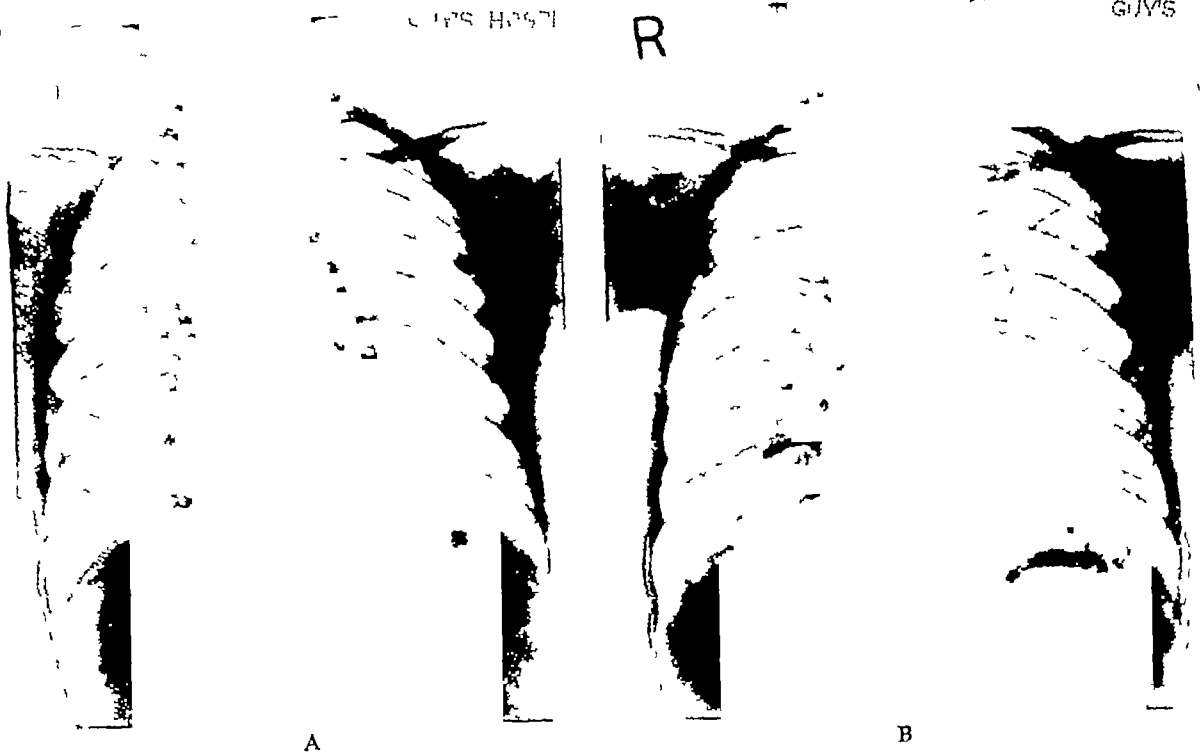
FIG 13 —Case 29, a boy aged 10, with Fallot s tetralogy

(A) Before operation showing a blunt apex and a fairly large pulmonary bay

(B) Four months after operation showing hardly any increase in the size of the heart (c t r unchanged at 52) although the anastomosis was most successful, as shown by his improved ability to get about and the improved colour   The pulmonary artery is more prominent on the right which was the side of the anastomosis as the aortic arch was left sided

TABLE III

CARDIO-THORACIC RATIO BEFORE AND AFTER
BLALOCK-TAUSSIG OPERATION

| Number of cases | Before opera tion | After operation | | | Time after opera- tion |
		About one month	About four months	At last visit	
13	47 2	51·0	51 8	52 5	12 mo
22	48 6	50 9	—	52 8	6–11 mo

the 35 cases   It had increased by 2 to 3 points per cent (from 48 to 50 or 51) in 8, by 4 or 5 points per cent in 10, by 6 to 8 points per cent in 10, by 10 points per cent in 1, and by 12 points-per cent in 1

case   In the last two the hearts had been small before operation (c t r 41 and 44)

Only one patient (Case 33, Fig 14) has made us anxious about his future by the degree of increase in the size of his heart   His clinical improvement was as much as in the others and there was difficulty in restraining him from doing everything   He was treated as a normal child at school except for games and had nothing except occasional attacks of tachycardia *

PULMONARY VALVULOTOMY

During the same period 6 patients have been submitted to the operation of pulmonary valvulo- tomy   Four of these were thought to have Fallot's tetralogy with pulmonary stenosis as an important feature and the other two were thought to have pure pulmonary stenosis with some degree of patent

* We have since heard that eight months after operation he developed bronchitis with a temperature of 103 degrees, œdema of the legs soon followed, the temperature persisted, and he died in a few days

<div align="center">A   B</div>
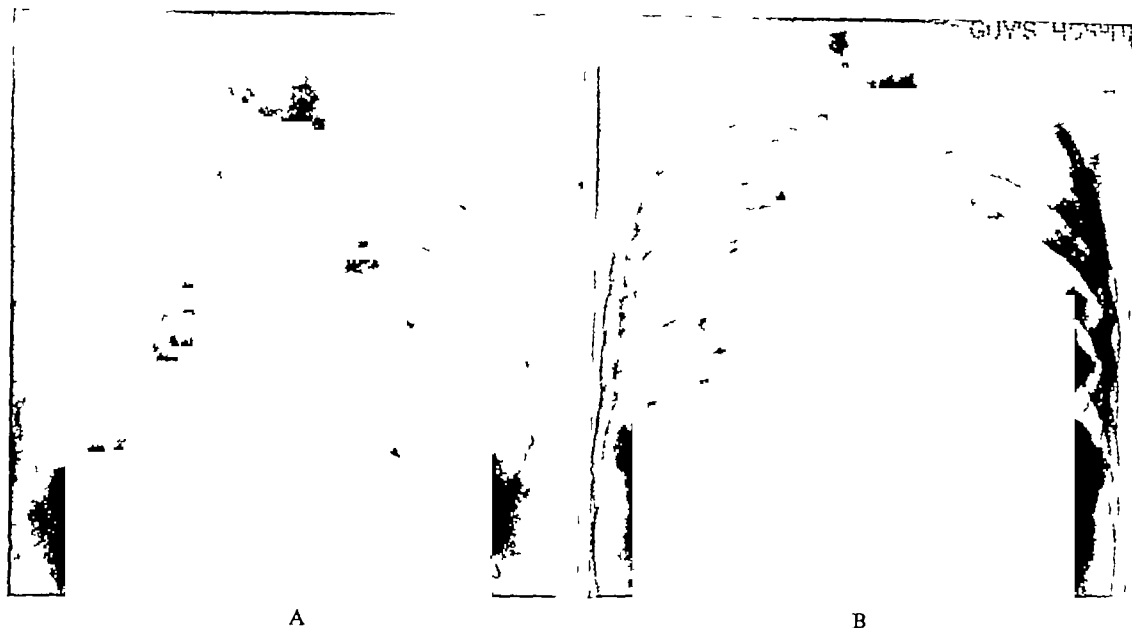
FIG 14 —Case 33   From a boy aged 4, with tricuspid atresia and non functioning right ventricle

(A) Before operation showing an enlarged and rather horizontal heart

(B) Five months after operation illustrating the greatest increase of heart size seen so far in any patient after operation, the c t r having increased from 61 (11 0/18) to 69 (13 0/18 75)   The pulmonary artery had become more prominent on the right, the side of the anastomosis, as the aortic arch was left-sided

foramen ovale or auricular septal defect   The operation appears to be of much greater danger and three (Cases P031, H117, and H121) of these six have died, but they were all older patients, 22, 24, and 29, and this and the relatively small numbers make any exact comparison impossible

In the remaining three, the operation was successful and the patients were considerably improved in colour and in their ability to move about without acute dyspnœa   Unfortunately, two of these were handicapped, one by hemiplegia (Case H109) and one by some disability of the leg from arterial embolism (Case P079)   Whether this is a greater risk with valvulotomy remains to be seen because here again, they were older cases, aged 18 and 23, and it appears that age (though it may be the associated degree of polycythæmia) makes thrombosis and embolism a greater risk

The remaining patient (Case H107, Case 2, Brock, 1948), a girl aged 11, was as brilliantly successful as any with an anastomosis   She was active all day and was able to walk several miles and looked a normal colour with only trivial or even doubtful cyanosis on careful examination   Her arterial O₂ saturation had increased from 81 to 91 per cent   Twelve months after operation, she has developed no signs suggestive of pulmonary regurgitation

SUMMARY AND CONCLUSIONS

The method of chosing the first 50 patients for the Blalock-Taussig operation at Guy's Hospital and the results obtained have been described   Three cases were thought to have tricuspid atresia with a non-functioning right ventricle, and all the others Fallot's tetralogy, though sometimes with a known or suspected complication   All had great disability and severe or moderate cyanosis dating from birth or early infancy, with polycythæmia and clubbing of the fingers

Most of these patients had a systolic murmur—often not very loud—in the pulmonary area, and in about half of them a thrill could be felt at this site None had a diastolic murmur or a greatly accentuated second sound   Four-fifths of the patients squatted habitually and panting on exertion was nearly as characteristic

The heart was generally within normal limits though some right ventricular hypertrophy could be seen on cardioscopy and shown electrocardiographically, sometimes the heart was small, and

occasionally a little, but never much, enlarged   If the cardio-thoracic ratio is under 45, the heart will probably stand a fairly large anastomosis with still greater improvement for the patient   More experience will be needed to decide how much enlargement of the heart may be allowed   slight enlargement with the c t r 52 to 54 should certainly not contra-indicate operation but larger hearts with the c t r 55 and above require special consideration and the improvement may not be so lasting

The heart was sometimes sabot-shaped and sometimes of more normal shape with a straighter left border or even with a slight prominence of the pulmonary region   The pulmonary vascular shadows were generally much diminished though sometimes more mottled shadows, probably produced by the collateral circulation, made this decision difficult

The pre-requisite of a successful operation is that the disability and cyanosis should be mainly due to an inadequate blood flow to the lungs and, in general, this is indicated by the clinical and radiological findings that have been given

The other prerequisites are that there should be a suitable systemic artery and a pulmonary artery large enough for an adequate anastomosis   Angiocardiography helps with both these points by showing the anatomy of the aortic branches and of the pulmonary artery and so in helping one to plan the details of the operation that is most likely to be feasible and successful   Careful radioscopy should generally be able to decide about a suitable pulmonary artery

The operation was usually an end-to-side subclavian-pulmonary anastomosis on the side opposite to the aortic arch   The aortic arch was right-sided in a quarter   Reasons have been given for thinking it is better to operate on the left side regardless of the side of the aortic arch and this has become the usual routine recently   Our conclusions about the surgical procedure that should be adopted have been summarized (page 188)

The immediate upset caused by the operation is less than might be expected and children stand it well and recover quickly   Morphia should be used in small quantities only, and intravenous fluids are not needed in large amounts, though fluids should be taken freely by mouth before and after operation   Breathing exercises should be started at once and carried out vigorously   The only complications that are at all common are pulmonary—some collapse of the lung and pleural effusion   These generally clear up quickly though they often need aspiration once and may sometimes be slower and cause trouble   Arterial thrombosis at

the time of operation or soon after has been the second main complication and as already stated two of these patients have been left with some residual disability   This risk seems greater when the polycythæmia is severe

On the average the temperature had settled to normal by the third day, and excluding 12 cases where there were complications from cerebral thrombosis, wound sepsis, or pleural effusion, the patient was up and getting about the ward on the eighth day and was able to leave hospital after 23 days

There were 7 deaths in these 50 cases—a mortality of 14 per cent   There were 3 others where no anastomosis could be performed

Of the remaining 40, there were 3 where we thought the improvement of little or no significance, and 4 where we have only classed it as fair, though in 2 of these the result was excellent as far as the heart was concerned but was marred by some residual disability from thrombotic hemiplegia

In 33 of the 50 cases (66 per cent) the results were almost perfect and the patient was able to get about all day and walk up to 5 or 6 miles instead of a few hundred yards or less   The cyanosis almost disappeared except slightly in the nails and on a cold day   Many children quickly started at ordinary schools, and cricket, camping, and roller skating became the occupations of some who had before been invalids doing hardly anything

A murmur similar to that of a patent ductus arteriosus was heard on the side of the operation in the successful cases   After operation with the added work of the heart from the new left to right shunt the heart generally increased in size a little but not greatly   In 5 of 35 cases there was no significant increase, in the remainder the cardio-thoracic ratio rose from 48 0 per cent to 50 9 when the patient left hospital and to 52 7 per cent when they were last seen (generally after 7 to 14 months)   Although these average figures might look like a progressive, if slow, increase, individual cases show that the greater part of the increase had generally taken place in the first 4 to 6 weeks   Only one patient so far—and he had tricuspid atresia—has caused us any anxiety for the future by the size of the increase in his heart, and symptomatically he has improved as much as the others

It was particularly encouraging that none of the patients seen a year after operation had failed to maintain or increase all the improvement they had made at the earlier follow-up after a few months

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APPENDIX ON CARDIAC CATHETERIZATION

BY G A ZAK

Nine of these cases underwent cardiac catheteriza-tion   Most were investigated when the procedure was still at an early stage of development at this hospital, with increasing skill and improved tech-nique the results in later cases have been more complete

In view of the envisaged operation the main object of venous catheterization was to get informa-tion regarding the pressure in the right ventricle and pulmonary artery, the presence and localization of shunts, and the volume of the pulmonary blood flow in relation to the height and weight of the patient

It is not intended to discuss the problems and findings of cardiac catheterization in detail   From the rapidly growing data on this subject several widely accepted facts have emerged   For example the pres-ence of blood of significantly higher oxygen saturation in the right auricle than in the venæ cavæ indicates arterial blood passing from the left auricle through an auricular septal defect, and the sudden fall in pressure from a high to a low level on passing from the right ventricle to the pulmonary artery is the best evidence of pulmonary stenosis   To calculate the pulmonary arterial flow with the aid of the Fick principle mixed venous blood must be obtained, and the mixing of the venous blood from the various sources may be incomplete in the right auricle   If the catheter can not be got into the pulmonary artery a blood sample obtained from the outflow tract of the right ventricle can be substituted   The pul-monary arterial flow is not necessarily equal to the total pulmonary flow (pulmonary capillary flow) as an appreciable amount of blood may reach the alveolar capillaries by way of a collateral circulation No attempt has been made to assess this

The sudden fall from high to low pressure on passing from the right ventricle to the pulmonary artery and sometimes the feel of release from a grip on the catheter is the best evidence of pulmonary stenosis, and a decreased pulmonary arterial flow is confirmatory evidence   If it is not possible to reach the pulmonary artery with the catheter, a high pressure in the right ventricle and a decreased pulmonary flow may be taken to lend good support to an assumption of pulmonary stenosis in the absence of clinical signs of mitral stenosis or heart failure

The magnitude and direction of an overall intra cardiac shunt is calculated by deducting the pul monary arterial from the systemic blood flow or vice versa   The adjective " overall " is used to denote that in many instances there is actually a to-and-fro movement of blood from the two sides across a single septal defect but as a rule one com ponent is larger to such an extent as to dominate the clinical picture

An evaluation of the output of each of the two ventricles of the heart, and the consequent calculation of a possible shunt is an approximation only   The calculation of the pulmonary arterial flow is often the more reliable   Of the three components neces sary for its computation, the O_2 uptake through the lungs and the O_2 content of the mixed venous blood are known   If the degree of the arterial oxygen saturation is normal the pulmonary venous blood is taken to be of equal saturation   Even if it is lowered one is justified in assuming the pulmonary venous blood as still being 95 to 98 per cent saturated with O_2 This was shown to be true by other investi gators in the absence of pulmonary conditions likely to interfere with the gaseous exchange in the alveoli

Case No , Age and Date of catheterization	Pressure (mean) in mm Hg from the skin of the back			Systolic B P (clinic ally)	Degree of O saturation percentages				Output in % of the average output of 3 0 l per min per sq m of body surface		Hb % 100% =15 6 g Hb	Surface area in sq m	O₂ consumption in ccs per min at S T P (B M R)
	RA	RV	PA		RA	RV	PA	Syst artery	System	Pulm			
Case 23, 19 yr, 13/1/48	15	43	—	115	29 0	33 1	—	46 5	100	30	120	1 24	170 (−5 0)
Case 49*, 8 yr, 6/2/48	14	(27)	—	100	SVC 46 8	23 2	—	58 8	180	—	125	0 83	140 (−3 0)
Case 35 7 yr, 23/4/48	7	45	15	110	—	—	—	—	—	—	—	—	—
Case 36 17 yr, 12/5/48	12	—	—	122	60 0	—	—	83 0	85	—	118	1 42	200 (0 0)
Case 42*, 19 yr, 20/5/48	11	—	—	95	55 7	—	—	73 0	110	—	140	1 32	220 (−19 0)
Case 39 11 yr 25/5/48	16	44	—	100	47 7	—	—	55 6	250	—	143	1 00	185 (−4 5)
Case 48 27 yr, 4/6/48	15	50	—	115	38 2	46 6	—	62 7	90	35	153	1 77	250 (−4 0)
Case 44 11 yr, 15/6/48	10	40	10	110	67 6	60 7	60 1	71 8	110	45	160	1 01	165 (−5 5)
Case 46, 15 yr, 18/6/48	10	62	10	125	53 3	55 4	46 6	61 8	100	50	142	1 59	210 (−5 5)

* In these two cases the diagnosis was tricuspid atresia, in all the others it was Fallot s tetralogy

The systemic blood flow in cases of septal defects cannot, however, always be calculated with the same degree of reliability as the right ventricular output Here, the mixed venous blood component is the weak link in the chain Often there is evidence of imperfect mixing in the right auricle, the coronary vein as a rule adding blood very much lower in oxygen content The inferior vena cava in turn produces, generally speaking, more saturated blood than the superior vena cava A blood specimen obtained from the inferior vena cava, however, may not be of uniform composition on account of the nearness of the openings of the hepatic veins This fact makes the recognition of small atrial septal defects producing admixture of arterialized blood uncertain if one is to rely on the taking of single blood samples only Because of the errors involved in calculating the pulmonary and the systemic flow one must hesitate to diagnose a small overall right to left shunt on small differences, larger differences can however be taken as reliable

In these nine cases the clinical diagnosis was supported Such support was felt to be forthcoming in cases of Fallot's tetralogy if there was evidence of pulmonary stenosis and an overall right to left intracardiac shunt

Of the two cases diagnosed on clinical grounds as having tricuspid atresia only a single right chamber with normal right auricular pressure could be demonstrated and no evidence of an atrial left to right shunt were found In neither of these cases could the catheter be made to cross over to the left auricle

There was evidence of an overall right to left shunt in every case

The A–P diameters of the chest ranged from 18 to 24 cm with an average of 19 cm To obtain the pressure as measured from the sternal level 15 mm of Hg has to be deducted from the values given in this table

The catheterizations were carried out by Dr G A Zak and Dr H E Holling

Case 23 Pulmonary artery not entered as tip of catheter got caught in papillary muscles towards the base of the heart, without getting near the pulmonary valves

Case 49 Results vitiated by crying The superior vena cava value is substituted for the right auricular value, as the former followed a period of calmness It was thought at first that the right ventricle had been entered, but probably the catheter was in the coronary sinus, with the pressure high from partial occlusion of the lumen of the catheter

Case 35   The use of an inhalation anæsthetic made gas analyses of the blood specimens impossible The raised right ventricular pressure in conjunction with the lowered pulmonary arterial pressure indicates stenosis of the pulmonary ostium

Case 36   Venospasm led to abandonment of procedure

Case 42   Only the right auricle could be entered The tip did not pass into the left auricle through a possible atrial septal defect   If such a defect was present, a left to right shunt through it would appear unlikely on account of the S V C and I V C saturations, which agreed with the value found in the R A

Case 39   The right ventricle was only entered with difficulty and attempts at entering the pulmonary artery failed   Tip was at the base of the heart The pressure in the right ventricle was recorded but no blood specimen was obtained, and when on withdrawing the catheter too far this chamber had been left the permissible screening time did not allow further search for the right ventricle

Case 48   The pulmonary artery could not be entered though tip of catheter was brought to base of heart   Good agreement between S V C and right auricular saturation   The increased right ventricular saturation over the right auricular sample favours presence of a ventricular septal defect, giving rise to shunting of the blood in both directions though differing in quantity   The smaller opposing shunt can be detected if the tip of the catheter happens to be near such a defect, which seems to have been the case here

Case 44   Superior vena cava, 54 per cent, and inferior vena cava, 60 per cent saturated, favour a small left to right shunt through an atrial septal defect, which is, however, far outweighed by the large right to left shunt through a ventricular septal defect or overriding of the aorta

Case 46   Good agreement between the saturation values in both venæ cavæ, right auricle, and right ventricle   The low pulmonary artery saturation is thought to be due to obstruction by the catheter of an already narrowed ostium for about two minutes, prior to withdrawing the blood sample The pulmonary flow has been calculated from the right ventricular saturation

ABSTRACTS OF CARDIOLOGY

The Electrocardiogram in Biliary Tract Disease and During Experimental Biliary Distension Clinical Observations on 26 Patients G B Hodge and A L Messer *Surg Gynec Obstet*, 86, 617–626, May, 1948

The effect on the electrocardiogram of experimental distension of the biliary tract was investigated in 26 patients undergoing surgery of the biliary tract Sterile normal saline solution was introduced under pressure through a cannula into the gall bladder or through a rubber T-tube into the common bile duct, the maximum pressure used was 100 cm of water Twenty-two of the patients had chronic cholecystitis, 3 had previously had cholecystectomy, and 1 had a carcinoma of the head of the pancreas with chronic cholecystitis and cholelithiasis In 14 patients gall bladder distension and electrocardiographic studies were carried out simultaneously during operation Of a second group of 13 patients the common bile duct was distended in 12 and the gall bladder in 1 patient, without medication or anæsthesia, 10 or more days after operation No patient had angina or myocardial infarction and in none did distension of the common duct or gall-bladder cause anginal pain All patients who experienced pain during distension of the common duct or gall-bladder complained of respiratory distress during distension and in the majority the blood pressure rose No constant cardiographic changes were found as a result of the distension, control records obtained before operation included abnormal as well as normal tracings It is concluded that changes in the electrocardiogram in patients with biliary tract disease are variable and may be coincidental, and that it is not justifiable to speak of improvement of the cardiac condition as a result of biliary surgery on the basis of a single pre-operative and post-operative cardiogram, since serial tracing may show instability of the cardiographic pattern, especially of the T waves *A Schott*

The Changes in the Electrocardiogram Associated with Standing D Scherf and M Schlachman *Proc Soc exp Biol, N Y*, 68, 150–153, May, 1948

Records in 80 male patients without evidence of organic heart disease were taken in the supine position, after standing for 1, 5, and 15 minutes and again immediately upon resuming the supine position To investigate the part played by the sympathetic nervous system 0 5 mg of dihydrœrgotamine (DHE 45 ') was given intravenously to 12 patients and records were again taken supine and erect when the drug effect was at its height In 25 (31%) there were significant changes in the electrocardiogram on standing, but neither the kind nor the time of appearance of changes was uniform In 4

temporary A-V rhythm was observed as a result of change of posture In 11 out of 12 changes occurring immediately on standing could not be prevented by dihydroergotamine It is concluded that the immediate and delayed changes in the cardiogram must be ascribed to different mechanisms The former are due to the change of position of the heart and altered contact between the heart and neighbouring structures, the latter to the sympathetic nervous system acting on the heart directly or through the coronary arteries *A Schott*

A Clinical and Electrocardiographic Study of Paroxysmal Ventricular Tachycardia and its Management G R Herman and M R Hejtmancik *Ann intern Med*, 28, 989–997, May, 1948

In a heart that is damaged failure may be caused by sudden rapid rate Most hearts in which ventricular tachycardia develops have been previously damaged by coronary disease or digitalis A ventricular tachycardia is recognized by abnormally broad QRS complexes in the electrocardiogram along with an independent atrial rhythm

Twenty patients with ventricular tachycardia are reported of whom 14 had coronary disease with or without infarction The others had rheumatic heart disease, except for 2 in whom no organic disease could be found Nine of the 20 were receiving digitalis at the onset of the attack In 10 the heart rhythm reverted to normal on quinidine Quinidine by mouth in a single oral dose produces a maximum concentration in the heart in about an hour, being eliminated in 8 hours The largest dose used was a total of 5 2 g in 24 hours The method of Hepburn and Rykert of intravenous dosage is useful, 3 5 g of quinidine sulphate in 500 ml of 5% glucose intravenously at 100 ml per hour Once normal rhythm has been restored, quinidine should be continued by mouth for several days or weeks, the dosage being adjusted to prevent premature ventricular contractions Morphine intravenously has also been used successfully, 10 to 40 mg , repeated after half an hour to 2 hours Intravenous magnesium sulphate has also been used successfully The prognosis is that of the underlying cardiac disease In some cases achievement of a normal rhythm may not in itself prevent a fatal outcome *J McMichael*

Experience with the Schemm Regimen in the Treatment of Congestive Heart Failure. A A. Newman and H J Stewart *Ann intern Med*, 28, 916–939, May, 1948

The importance of a low salt intake in controlling œdema is now widely recognized It has even been shown that, provided the salt intake is low, large amounts

of fluid may be taken without increasing cardiac œdema Schemm carried this principle to the point of recommending a very high daily fluid intake with a diet low in sodium and yielding a neutral or acid ash residue Thirty patients were admitted to hospital for trial of this regime Failure to maintain a steady state of œdema during a control period led to the elimination of 21 patients from later analysis In only 9 were the data satisfactory The regime alone was without beneficial action Five of the patients were quite unable to consume the large amounts of water recommended Moreover, the diet was not liked by the majority of patients After an adequate trial of the Schemm treatment, the condition in 7 patients was found to be much improved on a regime of restricted salt, limited fluid and frequent administration of mercurial diuretics Analysing critically the charts in Schemm s papers, the authors do not think that diuresis was achieved on his regime The only occasions on which the patients lost weight were when mercurials were given   *J McMichael*

Aortic Stenosis   A Study of the Clinical and Pathologic Aspects of 107 Proved Cases   C W KUMPE and W B BEAN   *Medicine, Baltimore*, 27, 139–185, May, 1948

To facilitate the diagnosis of aortic stenosis the authors studied the clinical and pathological records of 107 postmortem examinations, in which aortic stenosis with calcium deposits had been demonstrated in the absence of any other valve lesion

The ages of the patients varied from 10 to 80 years, maximum incidence seventh and eighth decades, ratio males to females 3 to 1 A history of acute rheumatic fever was obtained in two-thirds Thirty four patients had chronic congestive failure, 10 had intermittent bouts of failure, and 19 gave a history of an abrupt onset of failure shortly before admission Cardiac pain was present in only 9 and syncope in 4 The pulse rate was accelerated Blood pressure was not characteristic On auscultation the aortic second sound was usually absent or diminished, a systolic murmur was heard at the base in 83% with transmission to the neck in less than half Basal diastolic murmurs were heard in one third of cases Similar systolic and diastolic murmurs were heard at the apex Basal thrills were felt in 33 cases and though usually related in intensity to the degree of stenosis they were absent in several severe cases Congestive failure was unusually refractive to treatment and was associated with much sweating Cardiac pain differed from typical angina pectoris in its lack of radiation or radiation to the right, its advent after, rather than during exercise and its resistance to nitroglycerin It was more closely associated with severe aortic stenosis than with coronary arteriosclerosis Death occurred suddenly in 21% of patients, usually after 5 to 30 minutes, in contra distinction to the instant death in some cases of myocardial infarction Coronary arteriosclerosis was common and was associated with myocardial infarction in an appreciable number of cases Arteriosclerosis was common in the abdominal and descending aorta but not in the ascending

The condition was diagnosed clinically in only 24% of cases, signifying too great an acceptance of the classical triad of basal systolic murmur, thrill, and small, slowly rising pulse   *W T Cooke*

The Diagnosis of Mitral Insufficiency in Rheumatic Children   A G KUTTNER and M MARKOWITZ   *Amer Heart J*, 35, 718–726, May, 1948

In order to assess the importance in rheumatic children of a loud blowing systolic murmur in the absence of demonstrable cardiac enlargement a comparison was made of the after-history of 144 children having such a murmur with that of 171 similar patients with potential and possible heart disease but with not more than a soft systolic murmur The average follow up period was 8 years (5 to 19 years) Those with the loud blowing murmurs were more susceptible to rheumatic fever as judged by the incidence of recurrences (63% had multiple attacks) than were the group with only potential rheumatic heart disease (31% had multiple attacks) Sixty nine (48%) of those with mitral insufficiency' developed organic heart disease, and 13 died of rheumatic infection and 7 of bacterial endocarditis Only 22 (13%) of the patients with potential rheumatic heart disease developed it and none died

These observations suggest that the diagnosis of mitral insufficiency, based on a loud blowing apical systolic murmur, is justified in children and carries a grave prognostic significance   *H E Holling*

Studies on the Coronary Circulation III Collateral Circulation of Beating Human and Dog Hearts with Coronary Occlusion   M PRINZMETAL, H C BERGMAN H E KRUGER, L L SCHWARTZ B SIMKIN, and S S SOBIN   *Amer Heart J*, 35, 689–717, May, 1948

Several methods of study were used in this investigation Red blood cells labelled with radioactive phosphorus were injected into moribund patients shortly before death At necropsy the heart was removed and the distribution of the radioactive cells was quantitatively determined by the Geiger counter and radio-autographs Five hearts were studied, 2 normal and 3 from patients with myocardial infarction who died 4 days, 12 days and 8 weeks after the onset of the attacks Despite certain criticisms that may be advanced against these observations, the authors conclude that in arteriosclerotic hearts with myocardial infarction in living man there is a functioning collateral circulation which allows blood to enter all parts of a myocardial infarction, including the central portions

Red cells labelled with radioactive phosphorus were injected into dogs at varying times after ligation of the anterior descending branch of the left coronary artery At various intervals thereafter the hearts were stopped suddenly by freezing The distribution of the radio active cells was quantitatively determined These observations lead the authors to conclude that (a) Blood from collateral channels supplies the entire mass of ischæmic myocardium distal to a ligated coronary artery (b) The ischæmic right ventricular myocardium supplied by the ligated artery is better nourished by collateral blood than is a similar portion of the left

ventricle (c) The sub-epicardial portion of the ischæmic myocardium is better nourished than the sub endocardial region (d) The anastomotic blood continues to enter the ischæmic myocardium for at least 30 minutes after coronary artery occlusion (e) The collateral blood supply to the ischæmic myocardium is an actively circulating one which supplies the entire ischæmic region

The observations are thought to explain in man (a) the rarity of infarction of the right ventricle, (b) the greater infarction of the sub-endocardial than of the sub-epi-cardial muscle, (c) the fact that infarcts are generally smaller than the mass of muscle supplied by the occluded vessel   *R T Grant*

The Effect of Occlusive Arterial Diseases of the Extremities on the Blood Supply of Nerves Experimental and Clinical Studies on the Role of the Vasa Nervorum J T ROBERTS *Amer Heart J*, 35, 369–392 March 1948

In a series of dogs the blood supply to nerves was interfered with in various ways—by ligation of the nutrient arteries, by stripping off the perineurium by compressing and stretching the nerve and by injecting air or particulate matter into the arteries The degree of ischæmia was assessed by the results of inter-arterial injections of dye The interference with blood supply was found to alter the function and structure of the nerves Clinical studies in man showed that the blood supply to peripheral nerves may be reduced by similar processes in a number of conditions Sensory and motor changes are closely related with the ischæmia of the nerves A reflex arc for explaining referred pain on the basis of neural ischæmia is proposed   *R T Grant*

The Effect of Arteriosclerosis on the Dynamics of Hypertension in the Aged A Preliminary Clinical and Pathological Study of 150 Cases F D ZEMAN and B M SCHWARTZ *J Gerontol*, 3, 40–47, Jan , 1948

The authors report clinical and necropsy findings in 150 unselected elderly subjects, observed for periods of from a few days to 20 years The maximum number of blood-pressure estimations on any patient was 57, the minimum 1 Blood pressure, taken during routine medical visits, was classified as normal (150/90 mm Hg), systolic hypertension (over 150/90 or under), systolic and diastolic hypertension (over 150/over 90) On this basis patients were placed in 4 main groups (1) (a) normal, 12% (b) mainly normal, occasional variations 11%, (2) (a) every systolic reading raised, with every diastolic reading normal 13%, (b) most systolic readings raised, with most diastolics normal, 26%, (3) (a) both pressures raised (except terminally), 17% (b) occasional variations of this, 11% (4) the remaining 9% in whom readings were variable One-third of all males had evidence of coronary occlusion In females the incidence was much lower Arteriosclerosis of the aorta was present in all groups but most severe in (2) Renal arteriosclerosis was most marked in group (3) Cerebral accidents became commoner as blood pressure rose

Necropsy showed that peripheral resistance increases with age, and this factor, with decreased aortic elasticity, gives rise to systolic hypertension, which may, however, really be a modified systolic-diastolic hypertension Pure systolic hypertension occurs when decrease in aortic elasticity is greater than increase in peripheral resistance The authors stress the need for consideration of cardiac cerebral and renal function before a blood pressure level is taken as indicative of cardiovascular disease, a normal blood pressure in old age is produced by interaction of the above variables, and does not afford evidence of normality   *Morag L Insley*

Heart Disease in Pregnancy D J MACRAE *J Obstet Gynaec Brit Emp*, 55 184–198 April 1948

Heart disease is a common and serious complication of pregnancy There was an incidence of 0 8% in 29,713 patients attending Queen Charlotte s Maternity Hospital from 1937 to 1946 inclusive, with a mortality of 3% In the series reviewed 11% of the maternal deaths were due to heart disease

Pregnancy increases the work of the heart to such an extent that a damaged heart may be unable to bear the extra strain The most valuable single method of assessing cardiac function in these cases is by determining the response to the routine of daily life The classification adopted by the New York Heart Association is recommended Group 1 no limitation of normal active life Group 2 slight limitation producing breathlessness at the end of effort Group 3 definite limitation necessitating resting two or three times while climbing stairs Group 4 heart failure at rest Auricular fibrillation is a most serious complication, in the series reviewed of 7 patients with fibrillation 3 died Once decompensation occurs in pregnancy the chance of its recurring in subsequent pregnancy is great, and termination requires consideration This is also advised for Group 4 patients and those in Group 3 who in the early months fail to respond to medical treatment This consists of maximum rest with at least 2 hours in the afternoon and 12 at night Weekly examinations are advised throughout pregnancy Intercurrent infection should be treated seriously, and admission to hospital for a week of observation at the twenty-eighth week is advised and again for the week preceding delivery Vaginal delivery is the method of choice with adequate sedatives and forceps in the second stage In Group 4 no obstetrical treatment should be attempted until the patient is thoroughly rested and digitalized

Cæsarean section was performed on 21 patients in this group, but its role in patients with heart disease is strictly limited, as for example in heart disease with associated disproportion The need for sterilization should not be used as an argument in its favour

In these 225 patients with heart disease 124 were suffering from mitral stenosis, 23 had an associated aortic incompetence and 13 had congenital lesions, of which the most serious was coarctation In such cases pregnancy should be avoided but if it does occur Cæsarean section is advised as the method of delivery

The avoidance of infection in the puerperium and the

importance of adequate rest are stressed, breast feeding was not permitted in Group 3 and 4 patients As most of the fatalities occurred in the puerperium the difficulty of giving a prognosis in the early stage of pregnancy is mentioned Patients may easily pass from one group to the other during the course of pregnancy or labour, but the prognosis has greatly improved with better antenatal and intra partum care *J Stallworthy*

The Electrocardiogram in Mitral Stenosis with Special Regard to its Development A Study of 100 Cases H RASMUSSEN and G NYHUS *Acta med scand*, 129, 446–471, Jan 27, 1948

The authors state that their object in this study was to seek electrocardiographic peculiarities, other than those usually described, that might be of value in diagnosis One of the authors believed that he had observed, in a previous study of the cardiogram in diseases of the left side of the heart, progressive changes leading to a left bundle branch block It was therefore possible that similar changes might be found in disease affecting chiefly the right side of the heart

Serial studies of the electrocardiograms of 100 patients and of the size of the heart show that the cardiographic changes and increase in the size of the heart appear simultaneously during the progress of the disease Retardation of the impulse to the right ventricle is held to be decisive for the cardiographic development The retardation may cease in the stage with low R_1 or may progress until a maximal right ventricular retardation curve appears, ending with right bundle-branch block The latter occurs in the same proportion of cases as does left bundle branch block in left heart disease

Donald Hall

The Arterial Oxygen Saturation in Cyanotic Types of Congenital Heart Disease G E MONTGOMERY, J E GERACI, R L PARKER, and E H WOOD *Proc Mayo Clin*, 23, 169–176, April 14, 1948

This communication deals with the application of the oximeter to measurements of oxygen saturation of the blood The oximeter used was that described by Millikan in 1942 and fitted with a photo-electric colorimeter The oxygen saturation of the blood is measured directly by fitting the apparatus on to the human ear The first study was concerned with the oxygen saturation of the blood in 25 patients with congenital cardiac defects of the cyanotic group, 19 healthy subjects served as controls Readings of oxygen saturation of arterial blood were taken and the effects of breathing 100% oxygen, change of posture, and exercise were particularly noted

With the patients breathing pure oxygen the arterial saturation increased by from 2 to 16 points %, while in the normal controls this was only increased by from 1 to 5 points The effect of walking less than 2 miles an hour diminished the arterial oxygen saturation by from 3 5 to 19 points % in the patients while the maximum in the normals was only 2 points %

Interesting data are given on 1 patient with the tetralogy of Fallot, who, when exercised on the treadmill for 5 minutes at 1 7 miles per hour, showed a fall of arterial oxygen saturation from 80% to about 50% in a normal subject in the same circumstances the oxygen saturation increased slightly

The second part of the paper deals with the determination of arterial oxygen saturation at rest and during exercise in 8 cyanotic patients This was done both by the Van Slyke method and by oximeter readings The results were then compared and it was found that the average decrease in saturation on exercise was 19 5% by the Van Slyke method, while the simultaneous oximeter readings indicated a 13 3% decrease Thus the discrepancies are large, but, as the authors say, "the instrument is still of considerable value in estimating the degree of disability of a patient and in judging the efficacy of corrective surgical procedures in such patients' Suitable data are given in support of these statements

A I Suchett Kaye

Electrokymographic Studies of Asynchronism of Ejection from the Ventricles Normal Subjects and Patients with Bundle Branch Block G F ELLINGER, F G GILLICK B R BOONE, and W E. CHAMBERLAIN *Amer Heart J*, 35, 971–979, June, 1948

Analyses of electrokymograms indicate that, in normal subjects, asynchronous ventricular ejection is more frequent than synchronous ejection In patients with left bundle branch block ejection from the right heart and in patients with right bundle branch block ejection from the left heart precedes that of the opposite side by a significantly longer time than in normal subjects

R T Grant

The Effect of Spinal Anesthesia on the Renal Ischemia in Congestive Heart Failure R. MOKOTOFF and G ROSS. *J clin Invest*, 27, 335–339, May, 1948 12 refs.

High spinal anæsthesia caused no significant changes in renal plasma flow and glomerular filtration rates in 11 cases of chronic congestive heart failure. The ischæmia with vasoconstriction associated with this condition cannot be attributed, therefore, to neurogenic stimulation following a fall in cardiac output

E F McCarthy

Oxygenation Studies in Congenital Pulmonary Stenosis. An Application of Recording Oximetry in the Evaluation of Cardiorespiratory Function G GULLICKSON, J O ELAM, H HAMMOND, J R PAINE, and R L VARCO. *Amer Heart J*, 35, 940–947, June, 1948

In 10 cases of the tetralogy of Fallot the arterial oxygen was estimated by a recording oximeter before, during and after operation for the establishment of a systemic pulmonary arterial shunt The chief findings were that (1) a rise in arterial oxygen saturation occurs practically immediately on the establishment of the shunt, (2) as a result of the operation the saturation time upon administration of 100% oxygen is greatly shortened

R T Grant

HYPERTENSIVE AND ISCHÆMIC HEART DISEASE
A COMPARATIVE CLINICAL AND PATHOLOGICAL STUDY

BY

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Hypertension and coronary sclerosis have been the subject of extensive study, yet they have many aspects that are still poorly understood In the present work we have tried to ascertain how far they are dissociated and how far they overlap, and in particular we have studied their effects on the circulatory capacity of the coronary tree by injection and radiography

Over a period of four years, from 1935 to 1939, we made a careful clinical study of most of the cases of ischæmic and hypertensive heart disease admitted to the wards of the Hammersmith Hospital A total of 189 cases was analysed, of which 55 per cent were hypertensive, 30 per cent were ischæmic, and 15 per cent were mixed Sooner or later some of these cases came to autopsy and so provided our chief material

Each patient was classified in an arbitrary fashion, on clinical grounds, before the necropsy was made those with angina pectoris or with myocardial infarction being considered to have ischæmic heart disease whatever the level of the blood pressure, those with high blood pressure and without angina or myocardial infarction being considered to have hypertensive heart disease

The diagnosis of angina pectoris was made entirely on the history, that of myocardial infarction rested on well-known electrocardiographic criteria Only patients with systolic blood pressures over 200 mm and diastolic blood pressures over 100 mm , known to have been persistent, were included in the hypertensive series In all there were twenty-seven hypertensive and fifteen ischæmic cases In addition, twelve normal hearts were included in the pathological study to serve as controls

In the hope of learning something about the factors governing cardiac enlargement, and in order to facilitate correlation between the clinical and pathological findings, an attempt was made to divide the cases into subgroups Subdivision of the fifteen ischæmic cases proved too difficult, however, and was finally abandoned in favour of Table I, for it was not clear whether a profitable subdivision should be based on the height of the blood pressure, on the duration of myocardial ischæmia, or on the duration of heart failure, moreover, the blood pressure was not known prior to myocardial infarction in some instances

The twenty-seven hypertensive cases, which followed a simpler course, were subdivided according to their stage of development when death intervened as follows

(1) No cardiac symptoms Cases 24, 47, 60 and 69 Death was from pulmonary embolism in Case 24, from cerebral hæmorrhage in Case 47, and from uræmia in Cases 60 and 69

(2) Effort dyspnœa only Cases 23, 36, 39, 43, 44, and 65 Death was from cerebral hæmorrhage in Cases 23 and 44, from herniotomy in Cases 36 and 39, from pneumonia in Case 43, and from hæmatemesis from peptic ulcer in Case 65

(3) Left ventricular failure Cases 11, 13, 19, 41, 45, and 68 Death was from cerebral hæmorrhage in Case 11, from uræmia in Cases 13, 19, 41, and 45, and from bronchopneumonia in Case 68

(4) Full course—death in congestive heart failure Cases 8, 32, 38, 58, 62, and 63 followed previous manifestations of left ventricular failure, Cases 28, 48, 49, 50, and 53 had no such previous manifestations

CLINICAL FEATURES

Owing to the arbitrary nature of the clinical grouping, the complaint was necessarily one of pain in those with ischæmic heart disease in ten it was the presenting feature, but in five it was less evident than dyspnœa For the same reason pain was not present in the hypertensive group, except in an

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TABLE I

ISCHÆMIC CASES

Case No	B P	Duration of angina (months)	Duration of myocardial infarction (months)	Duration of L V failure (months)	Duration of congestive heart failure (months)	Weight of patient
17	–	nil	<1	<1	nil	12 st 6 lb
22	+	24	24	24	nil	6 st 7 lb
25	–	24	10	nil	nil	—
29	+	30	<1	nil	nil	—
30	+	nil	20	18	1 5	8 st 7 lb
37	–	1	1 5	2 5	2 5	—
40	–	nil	9	8	nil	13 st 1 lb
42	++	18	nil	nil	nil	9 st 4 lb
46	+	24	15	terminal	terminal	10 st 0 lb
51	+	nil	<1	terminal	terminal	12 st 6 lb
52	–	24	24	3	3	10 st 2 lb
55	+++	12	nil	36	terminal	12 st 9 lb
66	–	60	<1	<1	terminal	11 st 0 lb
70	–	12	<1	<1	<1	—
73	+	6	1	1	1	—

Note —The blood pressure is recorded as + when it was in the region of 160–180/80–100 at its highest In Case 42 it was higher than this, but only for a short time, Case 55 was originally classed as hypertensive, but had to be transferred to the ischæmic group owing to the development of angina Case 37 was complicated by rheumatic heart disease with organic mitral incompetence

atypical form which will be described later, but dyspnœa was invariable in those with cardiac symptoms

There was a high incidence of rheumatic fever in both groups, four out of fifteen with ischæmic heart disease, and six out of twenty-seven with hypertensive heart disease In two of each group the first attack had been in childhood, but in the remainder it had occurred in the third and fourth decades, and from the description might well have been rheumatoid arthritis There was nothing else of significance in the previous history

Personal and family history The back-ground of these patients—their environment in childhood and later life, their private lives, their occupations, their relaxations, their habits and their reactions to the world in which they lived—seemed ordinary

Cardiovascular disease was described in one or other or both parents in four of the ischæmic and in three of the hypertensive patients, but its exact nature, whether ischæmic or hypertensive, could not be ascertained

Sex and age There were twice as many males as females in the ischæmic group, whereas the proportion was equal in the hypertensive group This difference is significant and well known It was even more conspicuous in the larger clinical series The sex distribution of the mixed cases was the same as of those with hypertension

In the ischæmic group the average age for the men was 57 and for the women 68, in the hyper-

tensive group the figures were 59 and 55 respectively The point of interest is the older age of women with ischæmic heart disease This, too, is now well known

Duration and onset The average duration of life from the onset of cardiac symptoms was 1 9 years for those with ischæmic heart disease, and 2 2 years for those with hypertensive heart disease Since the period during which these investigations were carried out was only about four years, and since only those cases that died were included in the series, these figures do not indicate the true prognosis of the diseases in question

Seven of the ischæmic cases began with angina pectoris, four with dyspnœa on exertion Of those with dyspnœa, one had rheumatic heart disease and another had hypertensive heart disease as well as occlusive coronary atherosclerosis Thus only two of those with pure ischæmic heart disease started their symptoms with dyspnœa

In the hypertensive group, on the other hand, seventeen out of twenty-three with cardiac symptoms complained first of breathlessness, the initial symptom was fatigue in four of the remainder, and dropsy in the other two

Course Six ischæmic patients recovered sufficiently after the onset of cardiac symptoms to resume work without distress The duration of this improvement was six months to two years The work undertaken was not light, and one of them worked as a navvy for a year after his first myocardial

infarction Thirteen out of the fifteen ischæmic cases developed myocardial infarction sooner or later, the two that died without this development were complicated, one by polycythæmia vera, the other by hypertensive heart disease Six patients had paroxysmal cardiac dyspnœa following myocardial infarction, and five of these later developed systemic congestion Two others had heart failure with systemic congestion without evidence of preceding left ventricular failure

In the hypertensive group recovery of function was rare after the onset of cardiac symptoms, and was observed in only two out of twenty-three patients Both experienced acute pulmonary œdema on unaccustomed effort, and subsequently recovered to the extent that they remained free from all symptoms for several months, even though they carried out their normal duties In the remainder the condition steadily deteriorated

The full course of hypertensive heart disease was witnessed in six patients effort dyspnœa progressed to left ventricular failure at rest, and this was followed by failure with systemic congestion The average duration of life after cardiac symptoms appeared was two years and one month, the range being six to forty-eight months

Five cases gave no history of orthopnœa or paroxysmal cardiac dyspnœa, but after a period of effort dyspnœa developed heart failure with systemic congestion Occasionally, the initial symptom was dropsy The average duration of life from the onset of cardiac symptoms was two years and five months in this group, the range being six to eighty-four months

Six patients died from non-cardiac causes at the stage of left ventricular failure—four from uræmia, one from cerebral hæmorrhage, and one from bronchopneumonia The duration of cardiac symptoms in this group was twelve months (1 to 24 months)

Six patients died from non-cardiac causes at the stage of effort dyspnœa—two from cerebral hæmorrhage, two following herniotomy, one from pneumonia, and one from hæmatemesis due to peptic ulcer The average duration of cardiac symptoms was two years and three months (1 to 84 months)

The remaining four cases had no cardiac symptoms Two died with uræmia, one from cerebral hæmorrhage, and one from pulmonary embolism

Thus the courses of ischæmic and hypertensive heart disease were similar in that left ventricular failure usually preceded failure with systemic congestion, they were dissimilar in that temporary recovery of function followed the onset of cardiac symptoms in about a third of the ischæmic cases, whereas steady deterioration characterized those

with hypertension It is interesting and important that only one patient initially classed as hypertensive was transferred later to the ischæmic group because of the development of angina pectoris or myocardial infarction

INCIDENTS IN THE COURSE OF HYPERTENSIVE HEART DISEASE

During the course of hypertensive heart disease certain events were observed that deserve special comment, for their significance was clinically obscure Pathological studies clarified some of them

Case 8 At one stage this man was severely constipated, and developed atypical chest pain followed by a lower blood pressure than usual, by a weaker cardiac impulse, and by left ventricular failure The electrocardiogram showed low voltage QRS complexes and flat T waves in all leads At necropsy, the heart showed marked left ventricular hypertrophy and weighed 695 g In the skiagrams the coronary arteries appeared to be slightly smaller than those seen in other hypertensive hearts of similar weight, and their outlines were rather irregular, there were, however, no points of severe narrowing The cardiac muscle showed patchy fibrosis at the base of the left ventricle posteriorly The attack may have been due to temporary coronary insufficiency (Master *et al*, 1947)

Case 19 For two years in this case there was frequent complaint of an ache behind the right shoulder, aggravated by exertion, and sometimes accompanied by a dull heavy ache in both arms Latterly it was never mentioned At autopsy, the left ventricle was hypertrophied and the heart weighed 480 g Skiagrams showed coronary arteries of good size and with smooth outlines There was no evidence of coronary narrowing nor of myocardial damage It is concluded that the pain was not ischæmic

Case 24 Six weeks before death this woman was seized with substernal pain, accompanied by pallor, sweating, cold skin, marked drop in blood pressure, and slight hæmoptysis Serial cardiograms revealed the characteristic pattern of massive pulmonary embolism The heart weighed only 340 g The coronary arteries were larger than normal There was no sign of coronary narrowing or myocardial damage The presence of a relatively recent massive pulmonary embolism was confirmed

Case 51 This man's symptoms began with acute pulmonary œdema after climbing some stairs He was admitted with the diagnosis of acute myocardial infarction, but there was no convincing evidence of this Cardiograms, however, were not obtained The heart weighed 495 g Skiagrams showed the coronary arteries to be narrowed with irregular

outlines   There was complete occlusion of the right recurrent branch, and a recent infarct at the base of the left ventricle posteriorly   The original diagnosis was correct and subsequent clinical judgment at fault

Case 38   While in hospital this patient had an attack of severe substernal pain   Pallor and coldness of the skin were associated, and pericardial friction was heard later   But the blood pressure did not alter, and there were no electrocardiographic changes   The heart weighed 738 g   There was an organizing fibrinous pericarditis   Skiagrams showed the coronary arteries to be large with smooth outlines   There was no narrowing and no myocardial damage   Pericarditis was responsible for the pain

Case 53   This woman had severe attacks of paroxysmal cardiac dyspnœa associated with syncope and substernal pain or choking   She also had attacks of left breast pain which radiated down the left arm and lasted two days   When the venous pressure was high she complained of præcordial tightness, this was twice relieved by venesection   The heart weighed 555 g   Skiagrams showed coronary arteries of good size with smooth outlines   There was no narrowing and no myocardial damage   Pain might have been due to transient coronary insufficiency associated with left ventricular failure

Case 63   After partial recovery from left ventricular failure this man was pulled up on effort by a choking sensation in the throat accompanied by vague præcordial pain   Dyspnœa always preceded this sensation   Rest brought quick relief   The heart weighed 900 g (the largest in the series)   The coronary arteries were greatly enlarged and showed smooth outlines free from any points of narrowing   Histologically the myocardium was healthy except for a few microscopic points of fibrosis at the apex and base of the left ventricle   The fibrosis was focal and of the type frequently seen with myocardial ischæmia   The findings suggest that in spite of their enlargement the coronary arteries may have been inadequate to supply the enormous bulk of cardiac muscle, and pain may have been due to relative coronary insufficiency

Case 65   This woman, during the last two months of her life, developed substernal pain on effort, radiating to the right side of the neck, to the axillæ, and passing down the inner sides of both arms to the elbows   It lasted ten minutes or so, and was associated with numbness and whiteness of the right hand for about twenty minutes   It was worse in cold weather, and was relieved by rest   The heart weighed 450 g   Skiagrams showed the coronary arteries to be of good size and free from narrowing   The myocardium showed no damage   Coronary spasm was probably responsible for the pain

It is concluded that atypical thoracic pain in the course of hypertensive heart disease may be due to relative coronary insufficiency associated with left ventricular failure, to coronary spasm, to massive pulmonary embolism, or to pericarditis

MODE OF DEATH

Thirteen of the fifteen ischæmic cases died from the disease itself—ten of them abruptly and, in a sense, unexpectedly, and the other three slowly in congestive heart failure

In contrast, only eleven of the twenty three hypertensive cases with cardiac symptoms died from heart disease   Only two died suddenly—one with a dissecting aneurysm of the aorta, the other while under the influence of too much digitalis   The other nine died slowly in congestive heart failure, and continuous cardiograms at the time of death in three of them showed that the mechanism was not ventricular fibrillation or sudden standstill, but a slowly increasing depression of conduction

SYMPTOMS AND SIGNS

Cerebral symptoms   Symptoms resulting from disturbances of the cerebral circulation, apart from Cheyne-Stokes breathing, which was associated with heart failure in both groups, were confined to the hypertensive cases, with the exception of one patient with ischæmic heart disease who had a stroke   The following conditions were noted   blurring of vision due to papillœdema (4 cases), sometimes progressing to blindness (2), severe headaches (6), mental deterioration (4), cerebral hæmorrhage (4), cerebral thrombosis (4), and hypertensive en cephalopathy (1)

Renal symptoms   Nocturia occurred in five of the ischæmic and in twelve of the hypertensive cases   Uræmia developed in six of those with hypertension, but not in the others

Peripheral vascular symptoms   Two of the hypertensive group exhibited the Raynaud phenomenon, and one intermittent claudication   Symptoms of peripheral vascular disease were not present in the patients with ischæmic heart disease

Body-weight   In the ischæmic group body weights ranged from 6 stone 7 pounds to 13 stone 7 pounds, and on the whole were average   Of the women, two were unduly obese and two were unduly thin, of the men only one weighed more than 13 stone

In the hypertensive group, six patients were very obese, their weights ranging between 14 and 22 stone   In twelve cases there was considerable loss of weight (1 to 7 stone)

Cardiac rhythm   The rhythm was normal in ten of the fifteen ischæmic cases   permanent auricular

fibrillation was present in one, paroxysmal auricular fibrillation in three, paroxysmal auricular flutter in two, and paroxysmal tachycardia in one   These seven rhythm changes occurred in five different patients   The fact is stressed that permanent auricular fibrillation occurred in only one case, indeed it only occurred once in the larger clinical series of fifty-six cases

In the hypertensive group the rhythm was normal in twenty-one instances, auricular fibrillation occurred in the remaining six and was permanent in five of them   Other rhythm changes were not observed   Permanent auricular fibrillation occurred in 10 per cent of the larger series

Of the six patients with auricular fibrillation, four had heart failure, or, putting it in another way, four out of eleven patients with heart failure had auricular fibrillation   Again, out of sixteen hypertensive patients without heart failure, only two had auricular fibrillation

Contrasting the two groups it is seen that auricular fibrillation is more common in hypertensive than in ischæmic heart disease

Cardiac impulse   The character of the cardiac impulse was described as forceful or thrusting in only three of the fifteen patients with ischæmic heart disease   Usually it was impalpable   In the hypertensive group, on the other hand, it was described as heaving in nineteen   This difference is considered significant and important

Valves   Apart from one patient with organic mitral incompetence, due to concomitant rheumatic heart disease, there were no valve lesions in the ischæmic group   Aortic incompetence, however, occurred in four of those with hypertensive heart disease   It might be better described as an aortic leak, and appeared to be due to dilatation of the aortic ring resulting from high blood pressure There was no peripheral vascular evidence of reflux and the diastolic blood pressure was not lowered   Seven patients had a mitral systolic murmur, and two had a soft mitral diastolic murmur Both types of murmur were attributed to dilatation of the left ventricle

Fundi   Apart from one patient with a combination of hypertensive and ischæmic heart disease and one with a single small exudate, the fundi were normal in the ischæmic group   In those with hypertension, on the other hand, marked hypertensive retinopathy with papilloedema, exudates, and haemorrhages occurred in seven instances, exudates and haemorrhages without papilloedema in one, and either exudates or haemorrhages alone in two others

It may be concluded that significant changes in the fundi are part of the hypertensive picture and do not occur in association with ischæmic heart disease in the absence of diabetes (there were no such cases in this series)

Peripheral arteries   In eight out of the fifteen ischæmic cases the peripheral arteries were hardened Eleven of the twenty-seven patients with hypertension had similar vessels, in the remainder the arteries were unduly firm and rubbery, but could not be described as hard

X-ray appearances   The hearts of ischæmic cases were enlarged only when there was evidence of past or present failure, hypertension, or some other form of heart disease   Since only one patient had permanent auricular fibrillation it is not possible to comment upon the effect of this rhythm on the size of the ischæmic heart, for in that one case there was concomitant rheumatic heart disease with organic mitral incompetence   No instance of cardiac aneurysm was observed, but absence of pulsation in the region of the infarct was sometimes noted   Following heart failure (all those with failure had myocardial infarction), an enlarged cardiac shadow was always seen, the left ventricle being mainly involved

In the hypertensive group the largest heart shadows were those associated with congestive failure   Cases without symptoms, or with effort dyspnoea only, showed slight to moderate enlargement of the left ventricle

It is concluded that uncomplicated ischæmic heart disease does not cause cardiac enlargement, that uncomplicated hypertension causes hypertrophy of the left ventricle, and that heart failure is responsible for maximum cardiac enlargement in both groups

Electrocardiograms   In the ischæmic group cardiographic changes were those of myocardial infarction when present   The features indicated anterior infarction in the first instance in seven, and posterior in four   Two showed signs of both anterior and posterior infarction, and two had normal curves

In the hypertensive group sixteen out of twenty-four showed left axis deviation with depression of the RS–T segment in lead I, and of these eight also showed inversion of the T wave in lead I, and three inversion of the T wave in leads I and II   Two patients had left bundle-branch-block   Two had left axis deviation without other changes   In the remaining four there was no axis deviation but there was inversion of the T wave in lead I (Case 49), in leads I and II (Case 8), in leads II and III (case 69), and in leads I, II, and III (Case 19)   All those with heart failure showed significant changes

It is concluded that left axis deviation with depression of the RS–T segment with or without inversion of the T wave in lead I, or in leads I and II, is the

typical cardiographic pattern of severe hypertensive heart disease this pattern was not observed in a single case of myocardial ischæmia In cases of old-standing anterior myocardial infarction with persistent inversion of the T wave in lead I, there was no depression of the RS–T segment

The hypertensive pattern with T I inverted was found in a third of the hypertensive group and in two out of twenty-eight mixed cases in the larger clinical series

Blood pressure The average blood pressure of six ischæmic cases prior to myocardial infarction was 180/95 after infarction the average pressure in eleven cases was 125/80 In the majority many readings were obtained the highest average figure following infarction was 160/110 In two patients the blood pressure was taken immediately after an attack of myocardial infarction and was found to be elevated in both these cases it dropped slowly following the initial rise and did not reach its lowest level until the third or fourth day This delayed fall of blood pressure following myocardial infarction, with or without an initial rise, has been observed repeatedly in other cases in the clinical series Attention is drawn to this fact and also to the frequency of moderate elevations of blood pressure found in ischæmic heart disease prior to myocardial infarction, elevations that are rarely accompanied by enlargement of the heart Of fifty-six cases in the clinical series the blood pressure was less than 165/95 in 74 per cent

The blood pressures of the hypertensive cases were necessarily high owing to the arbitrary classification employed The average range was 245/140–190/115 The highest individual figure was 300/170, and the lowest 110/80 There were several features of interest

First, there was no case in which the blood pressure was observed to drop as a result of heart failure A terminal fall was common, but heart failure had often preceded this by weeks, months, or years

Secondly, when the blood pressure fell much there was usually an obvious cause This was hæmorrhage in one case, shock from a strangulated hernia in another, massive pulmonary embolism in a third, and impending death in two others

Thirdly the onset or cessation of auricular fibrillation, which was observed in Case 38, did not effect the blood pressure, whether there was heart failure or not (when there was fibrillation the pressure recorded was that at which most of the beats came through, and not the maximum pressure which was always higher)

Fourthly, two patients usually had normal pressures when at rest in bed, whether in heart failure or otherwise, but when up and about the figures

climbed to over 200/110 with or without heart failure One of these patients lived for seven years following the onset of cardiac symptoms—a record for the series

Renal function No case of pure ischæmic heart disease was complicated by serious impairment of renal function as judged by urine concentration and by the urea clearance test In the whole ischæmic group there was only one case with bad renal function, and that was a case with associated hypertensive heart disease Even albuminuria was very rare apart from heart failure

The hypertensive cases, on the other hand, frequently showed considerable impairment of renal function, and six of them died with uræmia Twelve out of twenty-seven had less than 44 per cent of normal renal function as judged by the urea clearance test Albuminuria occurred in all but one, granular casts were found in seven, there was considerable impairment of urine concentration in ten

It may be concluded that impairment of renal function is a feature of the hypertensive state, and is unrelated to ischæmic heart disease

Blood count There was not a single case with anæmia in the ischæmic group, but there were two with polycythæmia In contrast to this, nine hypertensive patients were anæmic, the red cell count being under 4,000,000 per c mm , or the hæmoglobin being under 60 per cent

DIFFERENCE BETWEEN ISCHÆMIC AND HYPERTENSIVE HEART DISEASE

The chief differences between ischæmic and hypertensive heart disease are shown in *Table II* The evidence is based on the clinical features alone, and will be reviewed later in the light of the autopsy findings which were not known when the table was compiled

PATHOLOGICAL FINDINGS

To obtain the desired pathological information, a technique had to be devised that would enable us to form an accurate estimate of the capacity of the coronary lumina during life, to trace the exact position of any vascular or myocardial lesions, and to preserve the tissues for histological study It was decided that these requirements would be met by injecting the coronary arteries with a radio-opaque gel, followed by radiography and subsequent clearing of the whole heart after the method of Gross (1921) In order that the degree of vascular distension should be comparable with that obtained during life, all cases were injected at the known diastolic pressure of the patient The only

TABLE II

The Chief Differences between Ischæmic and Hypertensive Heart Disease

Feature	Ischæmic cases (15)	Hypertensive cases (27)
Complaint	Pain	Breathlessness
Sex	Male female=2 1	Male female=1 1
Age	Males av 56 5 years	Males av 59 2 years
	Females av 67 8 years	Females av 54 6 years
Onset	Dyspnœa in 20%	Dyspnœa in 75%
	Usually pain	Sometimes fatigue or dropsy
Course	Temporary good recovery in 40%	Temporary good recovery in less than 10%
	Myocardial infarction in 13 out of 15	Development of infarction necessitating change of classification—1 case
Mode of death	Cardiac death 13/15 (abrupt 10/13)	Cardiac death in 11/23 (abrupt 2/11)
Symptoms from disturbances of the cerebral circulation	Rare apart from cerebral thrombosis	Blurring of vision 4
		Blindness 2
		Severe headaches 6
		Mental changes 4
		Cerebral hæmorrhage 4
		Cerebral thrombosis 4
Renal failure	Very rare	Six died with uræmia
	Renal function tests usually good	Van Slyke less than 44% in 12 out of 27
	Albuminuria rare apart from heart failure	Albuminuria in all but one
Fundi	Normal in all but one	Hypertensive retinopathy in 10 out of 27
Blood count	Anæmia did not occur	Anæmia in 9/27
	Polycythæmia in 2	
Rhythm	Permanent auricular fibrillation 1	Permanent auricular fibrillation 5
Cardiac impulse	Forceful or heaving in 3, usually impalpable	Heaving in 19, usually located with ease
Valves	Normal	Aortic leak in 4
Blood pressure	Average 180/95 before infarction	Av range 245/140 to 190/115
	Average 125/80 after infarction	
X-ray	Normal prior to heart failure	Slight to moderate enlargement prior to heart failure
	Always enlarged after development of heart failure	Considerably enlarged after development of heart failure
Electrocardiogram	Normal or typical changes of myocardial infarction	Left axis deviation with depression of the RS-T segment with or without inversion of the T wave, usually in lead I alone, sometimes in leads I and II, in 75%
	The pattern described in the hypertensive column was not seen in a single case	

exception to this was in the case of normal controls in which the blood pressure was not known In these cases a standard pressure of 90 mm Hg was used

The apparatus (Fig 1) consisted of a simple fluid column leading down from an adjustable container and connected to a mercury manometer This was filled with warmed normal saline and served to wash out the blood from the coronary vessels and also to supply the required head of pressure for injection The fluid column lead directly to a Y piece connected to two cannulæ for perfusing the heart, but was connected also to a shunt circuit containing two bottles, one to act as a pressure chamber and the other to contain the injection mass When this circuit was shut off, the apparatus perfused saline through the coronary vessels, but when the direct circuit was closed and the shunt circuit opened, the saline displaced the air from the pressure chamber into the bottle containing the injection

mass, driving the latter into the cannulæ The barium-gelatine injection mass was prepared according to the technique of Gross

Procedure At autopsy the heart was carefully dissected out, clots were dislodged and the heart weighed It was then placed in normal saline and left at room temperature until it was injected a few hours later (usually three hours) The proximal parts of both coronary arteries were then defined and under-run with ligatures Two cannulæ were then tied in, the whole manœuvre being carried out under water at 37° C This warmed the heart to body temperature and also prevented any bubbles entering the coronary arteries The heart was then perfused with normal saline at 37° C until the fluid issuing from the coronary sinus was relatively clear (about 1 minute) The circuit was then changed, and the warm gelatine mass injected at the same pressure When the mass could be seen to have entered the fine arterioles in the pericardium, the
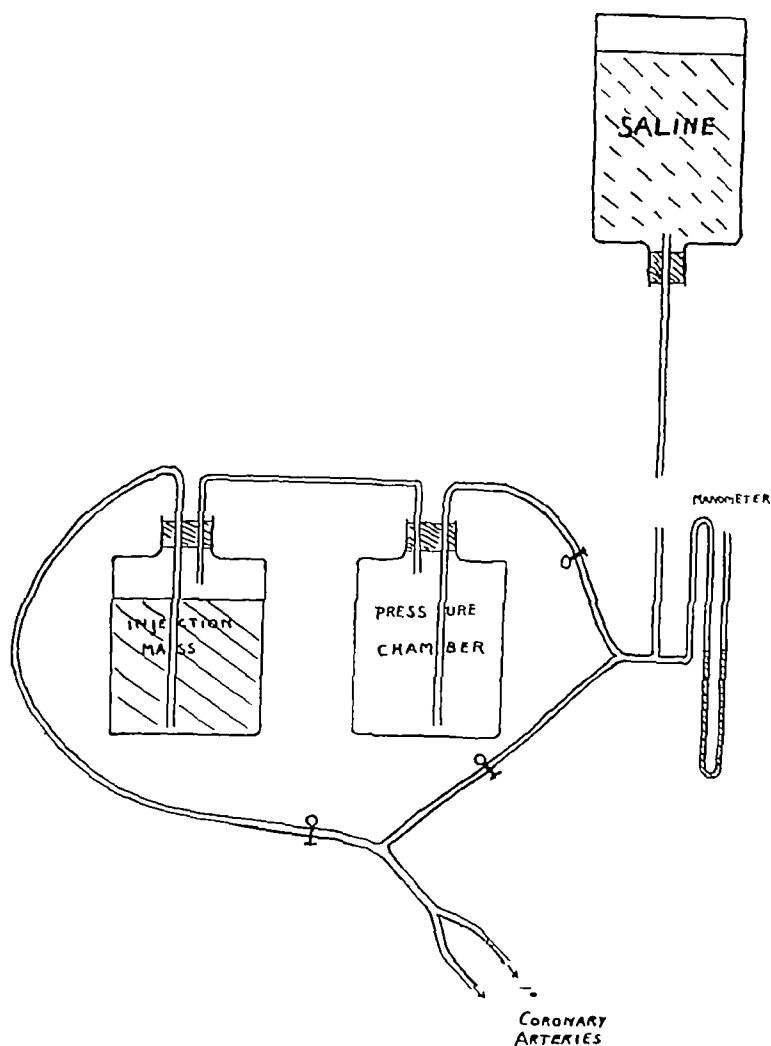
FIG 1 —Apparatus used for injecting the coronary circulation with barium gel
For description see text

heart was placed in iced water until the gelatine had set, and then transferred to a bath of formol-saline for 24 hours   Stereoscopic skiagrams were then taken according to standard technique   The heart was then returned to formol-saline and left to fix for about ten days   Next, four routine blocks of myocardium were excised and frozen sections stained for fat   These were taken from the apices of the left and right ventricles anteriorly and from the bases of the ventricles posteriorly   Special blocks were also taken from other sites as indicated   The heart was then passed through increasing concentrations of alcohol from 30 per cent to absolute alcohol, in steps of 10 per cent, remaining about three days in each bath   By this means complete dehydration was obtained in about three weeks

Old used alcohol was utilized for the lower concentrations, fresh absolute alcohol being employed only for the final one or two baths   This proved satisfactory and saved considerable quantities of alcohol   When the heart was dehydrated it was transferred to a bath of used methyl salicylate and later to fresh methyl salicylate   By this means the tissue was rendered relatively transparent   The coronary vessels, which stood out clearly owing to

the presence of the opaque injection mass, could thus be studied in detail and compared with their skiagrams

Blocks for section were then taken from the major coronary vessels (8 or more) and from the myocardium (5 or more) The myocardial blocks were obtained from five standard sites the anterior apical and posterior basal parts of the right and left ventricle, and the upper anterior part of the inter-ventricular septum Additional blocks were taken from any other sites that showed anatomical changes The blocks were washed in chloroform over night and embedded in paraffin

RESULTS

Normal controls Twelve normal controls, repre-senting each decade of life from the third to the eighth, were examined by the standard technique (Fig 3 and 7) In no case was there any evidence of heart disease or of high blood pressure either during life or at autopsy The details of the cases are given in Table III It is not proposed to discuss in detail the normal findings in injected hearts This has already been done by Gross (1921) and in so far as the normal anatomy of the coronary tree is concerned, our findings are in agreement with his

But we would add the important observation that coronary atheroma is compatible with an apparently normal lumen In all twelve of this series the skiagrams showed normal coronary outlines (Fig 3), yet coronary atheroma was subsequently discovered in five, and was severe in three In this connection it should be noted that the size of the coronary lumen in a paraffin section gives little or no indication of its real size during life It was repeatedly noted both in normal and pathological hearts that where sections showed coronary narrowing, skiagrams might reveal no abnormality

It is of course open to question how far such skiagrams reflect the state of the vessels during life, but we believe that, with the technique employed, they give the truest picture that can be obtained from an autopsy specimen In contrast to the pathological cases, normal controls with atheroma showed no trace of myocardial fibrosis

A second finding not emphasized by Gross was the relationship between the size of the coronary arteries and the size of the heart Since all skia-grams were taken by a standard technique the plates are comparable as regards size In all cases the three major coronary arteries (left anterior descending, left recurrent, and right) were measured near their origins From their diameters their total cross-sectional area was calculated and plotted against the weight of the heart The resulting graph (Fig 2) showed a fairly close scatter around a straight line, and indicates that there is a direct relationship between the bulk of the cardiac muscle and its blood supply

TABLE III
CONTROL CASES   SIZE OF HEART AND OF CORONARY ARTERY

Case No	Age	Sex	Heart weight (grams)	Total coron-ary bore (sq mm)	Coronary atheroma (microscopic)	Cause of death
12	22	F	225	27 9	—	Subarachnoid hæmorrhage
35	23	F	213	38 1	—	Polyposis coli
21	24	F	165	18 9	—	Carcinoma of colon
76	34	F	280	29 7	—	Carcinoma of stomach
72	39	M	282	36 5	±	Acute appendicitis
77	47	F	190	32 3	—	Carcinoma of cervix uteri
1	54	M	265	20 0	+	Seminoma of testis
14	55	M	200	28 7	+	Carcinoma of œsophagus
10	56	F	308	32 0	—	Bronchitis
64	61	M	365	59 0	—	Carcinoma of lip
26	73	F	310	39 4	+	Primary carcinoma of liver
27	80	M	400	36 5	±	Cirrhosis of liver

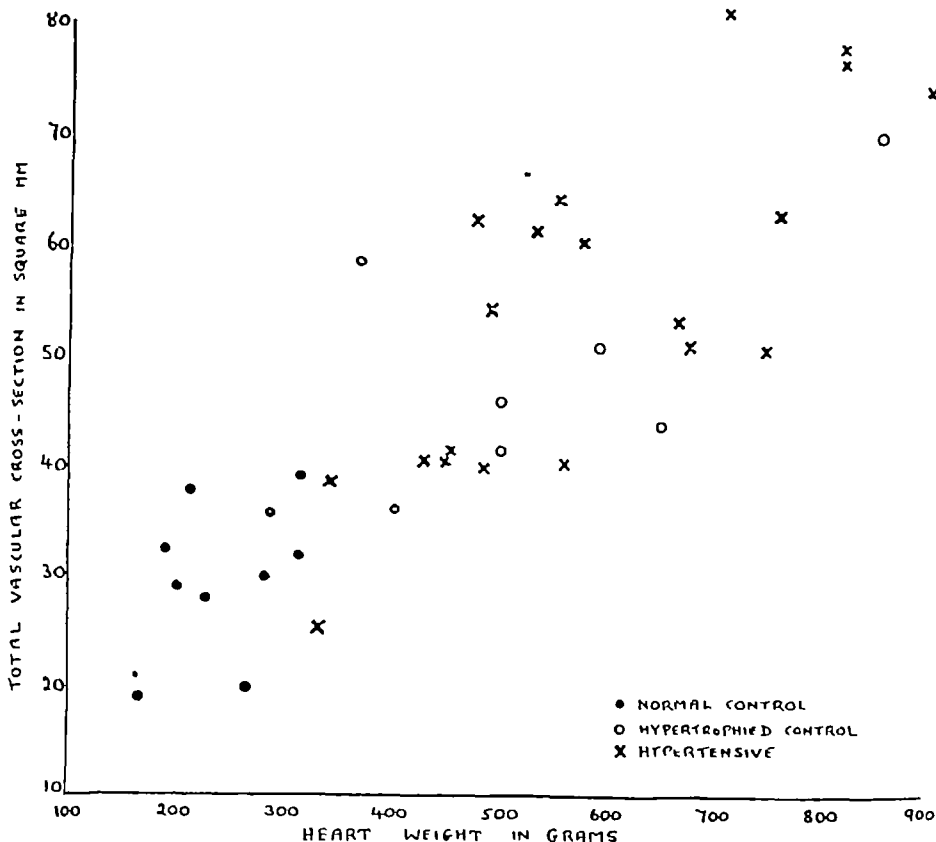|				*Hypertrophied controls*		
67	46	M	495	46 6	—	Cor pulmonale
71	60	M	495	41 8	—	Syphilitic aortic incompetence
54	71	F	585	51 5	±	Osteitis deformans Heart block
20	60	M	643	44 4	—	Rheumatic mitral and aortic disease
59	64	M	850	71 6	±	Rheumatic aortic incompetence

FIG 2—Graph illustrating the linear relationship between the heart weight and the total cross section of the main coronary vessels in normal controls, controls with hypertrophied hearts and in cases of hypertensive heart disease

HYPERTENSIVE GROUP

It soon became apparent that the pathological findings were totally different in the two types of case Though the differences in morbid anatomy and histology between ischaemic and hypertensive heart disease are well known, the dissimilarity was emphasized by the skiagrams The ischaemic hearts showed narrow coronary vessels with irregular outlines, and, as a rule, one or more complete occlusions (Fig 6, 9, and 10) The hypertensive hearts, on the other hand, showed large wide coronary arteries with smooth outlines and no narrowing There were a certain number that showed evidence of both hypertension and ischaemia

This group comprised twenty-seven cases of clinical hypertensive heart disease, subdivided into four groups according to their severity (page 205) The main pathological findings are summarized in Table IV

Heart weight All but two showed cardiac hypertrophy, the mean cardiac weight for the whole group being 597 g ±149 g It will be noted from Table IV that the degree of cardiac hypertrophy expressed as total heart weight is fairly closely related to the clinical severity of the disease judged by the functional state of the heart In the cases that ran a full cardiac course and died in congestive failure, the mean weight was 729 g In the cases that showed evidence of left heart failure but did not die a cardiac death, the mean heart weight was 585 g In those with effort dyspnœa only the mean weight was 492 g Finally, in the four cases with no cardiac symptoms, the mean weight was only 406 g

In all cases the increased cardiac weight was mainly due to left ventricular hypertrophy Right ventricular hypertrophy was difficult to estimate Owing to the hearts being cleared intact it was not

TABLE IV

HYPERTENSIVE CASES   SIZE OF HEART AND CORONARY ARTERIES

Died without cardiac symptoms

No	Age	Sex	Blood pressure	Heart weight (grams)	Total coronary bore (sq mm)	Coronary atheroma		Myocardial fibrosis		R V hyper-trophy	Mode of death
						X-ray	Micro	Retic	Focal		
24	63	F	260/120	340	39 0	—	+	—	—	+	Pulmonary embolism
47	63	F	250/130	485	55 2	—	—	±	—	—	Cerebral hæmorrhage
60	46	F	280/140	470	63 0	—	±	+	—	—	Uræmia
69	21	F	250/130	330	25 3	—	—	—	—	—	Uræmia

Died with effort dyspnœa

No	Age	Sex	Blood pressure	Heart weight (grams)	Total coronary bore (sq mm)	X-ray	Micro	Retic	Focal	R V hyper-trophy	Mode of death
23	44	F	225/130	425	41 1	—	—	±	—	±	Cerebral hæmorrhage
36	58	F	220/135	545	64 8	—	±	+	—	±	Herniotomy
39	68	M	210/100	525	62 0	—	±	—	—	—	Herniotomy
43	87	F	230/150	440	—	±	±	—	+	—	Pneumonia
44	49	M	290/140	570	60 8	—	±	—	—	±	Cerebral hæmorrhage
65	44	F	230/120	450	42 3	—	±	±	—	—	Hæmatemesis

Died with left ventricular failure

No	Age	Sex	Blood pressure	Heart weight (grams)	Total coronary bore (sq mm)	X-ray	Micro	Retic	Focal	R V hyper-trophy	Mode of death
11	56	M	243/125	700	82 4	—	+	+	—	+	Cerebral hæmorrhage
13	67	F	260/125	447	41 1	—	±	+	—	—	Uræmia
19	42	F	260/160	480	40 6	—	±	—	—	—	Uræmia
41	64	F	280/145	575	—	+	+	—	—	±	Uræmia
45	54	F	260/120	660	53 8	—	±	—	—	+	Uræmia
68	67	M	200/125	650	—	±	+	+	—	—	Pneumonia

Died in congestive cardiac failure

No	Age	Sex	Blood pressure	Heart weight (grams)	Total coronary bore (sq mm)	X-ray	Micro	Retic	Focal	R V hyper-trophy	Mode of death
8	60	M	250/150	695	—	±	+	+	+	±	
28	69	M	150/120	750	63 8	—	±	+	—	+	
32	50	M	170/115	670	51 7	—	—	+	±	+	
38	53	M	270/140	738	51 5	—	+	—	—	+	
48	51	M	220/125	710	—	±	+	+	±	+	
49	54	F	200/100	810	79 3	—	±	+	±	+	
50	54	M	190/140	820	—	+	+	+	+	+	
53	59	F	190/110	555	41 1	—	±	+	—	+	
58	66	M	210/140	810	78 1	—	±	+	—	+	
62	68	M	220/135	560	—	+	+	—	+	—	
63	60	M	180/110	900	76 1	—	±	±	±	±	

possible to dissect off the right ventricle and weigh it separately, moreover, after clearing, it was considered that estimates of hypertrophy were of doubtful value owing to shrinkage   An attempt was made to estimate the degree of right ventricular hypertrophy histologically and the results are given in Table IV   Hypertrophy was obvious in fourteen cases, slight in four, and absent or unrecognizable in nine   The incidence of right ventricular hypertrophy in the different groups is of interest   In the eleven cases that died in congestive heart failure,

right ventricular hypertrophy was present in all but one   this one was complicated by severe coronary sclerosis   It is assumed that this hypertrophy was due to the strain thrown on the right heart by failure of the left ventricle

The same explanation may be given for cases of right ventricular hypertrophy in the second group, for although these patients did not die in congestive failure, they had evidence of left ventricular failure during life   In the other two groups there was insufficient left ventricular failure to account for

right ventricular hypertrophy   Case 43, however, was complicated by emphysema, and Case 24 by old pulmonary embolism   The remainder showed very slight, if any, hypertrophy   Apart from hypertrophy the myocardium appeared healthy in twenty-six cases   In the twenty-seventh (Case 62) there was macroscopic evidence of infarction

Endocardium   One (Case 48) showed calcifica-

tion of the aortic valve of Mönckeberg type, not causing appreciable stenosis or incompetence   All other cases were free from valve disease

Radiography

It will be most convenient to describe first the typical findings in this group and then to discuss the

FIG 3 —Normal control   Case 76   Heart 280 g skiagram of injected heart. Note size of coronary arteries and their smooth outlines   (All skiagrams are 0 6 of natural size and are comparable)

exceptions The most striking feature was enlargement of the coronary arteries (Fig 4 and 5) In 20 this enlargement was conspicuous the outlines of the coronary lumina were perfectly smooth and there was no suggestion of irregularity or focal narrowing The degree of coronary enlargement appeared to increase pari passu with hypertrophy of the heart When the three main coronary arteries were measured in the same way as the controls and their total cross sectional area plotted against the cardiac weight (Fig 2), a fairly close scatter around a straight line was observed, which proved to be a continuation of that previously described in controls This strongly suggests that the size of the coronary arteries is dependent on the size of the heart, and that they enlarge in response to
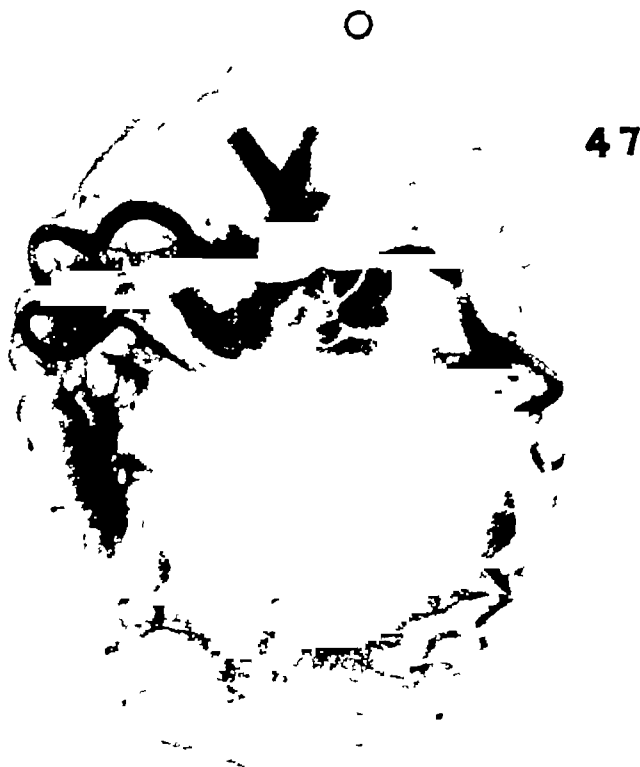

Fig 4 —Hypertensive heart disease Case 47, died before cardiac symptoms arose Heart 485 g. Note enlargement of heart and coronary arteries and the smooth outlines of the latter

an increased demand There is, however, an alternative explanation, namely that the coronary arteries are dilated by the raised pressure within them, or that the pressure at which they were injected caused them to dilate more than controls injected at lower pressure The latter possibility is refuted by the fact that two hypertensive cases (Cases 49 and 53) injected at low pressure (because the diastolic pressure had fallen some time before death) revealed coronary arteries as large as any injected at higher pressures

To investigate the possibility that coronary dilatation was the direct result of raised blood pressure during life, we injected five cases of cardiac hypertrophy due to other causes, namely, rheumatic valvular disease (Cases 20 and 59), syphilitic aortic

FIG 5 —Hypertensive heart disease Case 49, died of congestive failure Heart 810 g Note enormous heart and coronary arteries and the smooth outlines of the latter

regurgitation (Case 71), cor pulmonale (Case 67) and osteitis deformans (Case 54), all showed a degree of coronary enlargement similar to that seen in hypertensive heart disease (Fig 2) It is concluded that coronary vascular enlargement is related to cardiac hypertrophy

Seven out of the twenty-seven cases showed some evidence of occlusive coronary atheroma in the skiagrams In four (Cases 8, 48, 43, 68) this was slight, constituting no more than minor irregularities of outline and relatively small calibre in relation to the size of the heart, there were no points of gross narrowing In three of these cases the myocardium showed a few small foci of fibrosis in the fourth no lesion was detected Each of the other three (Cases 41, 50, 62) showed severe coronary sclerosis

FIG 6 —Ischæmic heart disease Case 66 Heart 565 g Note narrow irregular, calcified coronaries with several occlusions

with narrowing of the lumen, at least one complete occlusion, and evidence of myocardial ischæmia Clinically it is interesting to note that Cases 50 and 62 died suddenly   Case 41 died in uræmia

Cleared specimens   All cases were subjected to " clearing " in methyl salicylate, the cleared specimens (Fig 8) being compared with the skiagrams This confirmed the conclusions drawn from the latter and was of great value in selecting segments of the coronary vessels for histology It did not, however, add any further information Cleared specimens were not used for measurements owing to the shrinkage that occurs in the process of clearing.

Histology   *Coronary   arteries*   Twenty three cases (all but Cases 23, 32, 47, and 69) showed histological evidence of atheroma, yet the skia

FIG 7—Normal control   Case 35   Heart weight 213 g   Cleared specimen showing white injection mass filling lumen of coronary arteries   Note the perfectly smooth outlines

grams of sixteen of them exhibited normal coronary outlines, confirming the observation made in the controls that atheroma need not narrow the lumen Atheroma in these cases was relatively slight and of patchy distribution The seven cases that showed narrowing or irregularity of the arteries in the skia-grams all showed severe and generalized atheroma histologically Two other features deserve com-

ment In adult life normal coronary arteries have a well developed intima thicker than that of other arteries of similar size (von Glahn, 1936) In the hypertensive cases this layer tended to be thicker than in controls Secondly, the media was hypertrophied

An unexpected finding was polyarteritis nodosa in Case 32 This affected the majority of the small

FIG 8 —Hypertensive heart Case 36 Heart weight 545 g Cleared injected specimen showing dilatation of coronary lumen and smooth outlines, indicating absence of occlusive coronary atheroma

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arteries throughout the body, but most of the coronary vessels were spared

Histology   Myocardium   Evidence of hypertrophy has already been described   In addition, however, necrosis was seen in two cases   In Case 62 there were recent infarcts at both the apex and base of the left ventricle following severe coronary atheroma and thrombosis   In Case 41 there were numerous adjacent foci of infarction at the apex of the left ventricle, following thrombosis of the descending branch of the left coronary artery

Fatty change   Fatty degeneration of slight or moderate severity was found in fourteen out of the twenty-seven cases   It did not appear to be correlated with the size of the heart, with the state of the coronary circulation, or with any other known factor, and we have therefore been unable to attach any significance to it

Myocardial fibrosis was seen in the hypertensive cases in three forms, which we have called healed infarcts, focal fibrosis, and reticular fibrosis   The only example of a healed infarct was in Case 62 in which it was associated with an old coronary occlusion

Focal fibrosis took the form of small foci (under 1 mm) in which the muscle fibres had been replaced by collagen   In most cases replacement was complete, but occasionally necrotic muscle fibres were still visible   This lesion, which was seen with greater frequency and severity in the ischæmic group, occurred in seven of the hypertensive group (Cases 8, 32, 43, 48, 49, 50, and 63)   The skiagrams of four of these (Cases 8, 43, 48, and 50) showed coronary narrowing, but in the other three (Cases 32, 49, and 63) the coronary arteries had uniformly wide lumina and smooth outlines   Case 32 had polyarteritis and since some of the smaller vessels in the myocardium were involved (but not the main coronary vessels) it is fair to assume that fibrosis was the result of occlusion of small vessels   Cases 49 and 63 died in congestive failure, and fibrosis might be attributed to relative coronary insufficiency, but we must point out that the vessels were large and free from any obstruction

The third type of fibrosis, which we have called reticular, was always associated with gross muscular hypertrophy   It occurred in seventeen cases and took the form of an exaggeration of the normal interstitial reticular connective tissue fibres   In the normal heart these are extremely fine and can only be satisfactorily demonstrated by silver impregnation, but in cases of gross hypertrophy they thickened and became clearly visible as fine collagenous fibres surrounding the muscle fibres (Fig 11)   This form of reticular fibrosis tended to occur in foci and for this reason might be mistaken for ischæmic focal fibrosis   We believe, however, that it is a separate entity for the following reasons   Firstly, it was not seen in any of our pure ischæmic hearts,   secondly, it is limited to cases of gross myocardial hypertrophy,   thirdly, we were never able to demonstrate any sign of muscle loss   We consider that it is a form of concomitant fibrous tissue hypertrophy

Renal changes   The hypertensive cases were classified according to their cardiac condition, and though most were examples of essential hypertension, a few proved to be secondary to chronic nephritis   In practice the histological differentiation between nephritis and advanced arteriosclerotic kidney is extremely difficult, particularly since Ellis (1942) has shown that primary nephritis may persist with hypertension as the dominant clinical sign and arterial damage as the dominant renal change   In spite of these difficulties we have attempted to classify the kidneys in this series into hypertensive and nephritic   Seven (Cases 11, 19, 41, 47, 65, and 69) showed evidence of nephritis whilst the remaining twenty showed varying degrees of arterial damage, from a few hyaline vessels up to severe changes of the type classified as malignant hypertension   Six of the hypertensive group died in uræmia and four of these (Cases 19, 41, 45, and 69) were among those with histological evidence of nephritis   The other two (Cases 13 and 60) showed the histological appearances of malignant hypertension

ISCHÆMIC CASES

There were fifteen cases in this group, and their main pathological findings are summarized in Table V

Heart weight   The hearts were all hypertrophied except in Case 25   The mean weight for the whole group was 495 g $\pm$76 g , the range being 350–650 g   Such a degree of hypertrophy suggests that either ischæmic hearts may become hypertrophied during their course or that our cases were complicated by hypertension   It will be seen from Table V that eight cases had some degree of hypertension during life   The mean heart weight of these was 497 g , whilst the mean heart weight of those without hypertension was 494 g   Thus there is no correlation between heart weight and hypertension in this series   On the other hand, if the cases are divided according to the duration of cardiac failure, some correlation becomes apparent   Those with left ventricular failure for two months or more (6 cases) had a mean heart weight of 549 g $\pm$56 g , whereas those with terminal or no congestion (9 cases) had a mean heart weight of 459 g $\pm$60 g   The difference

TABLE V
ISCHÆMIC CASES

Case No	Age	Sex	Blood pressure	Heart weight (grams)	Coronary* occlusion site	Myocardial† Fibrosis	Necrosis	Mode of death
17	57	F	158/92	432	L D		L V A	Syncope
22	76	F	170/85	480	L D	L V A	I V S	Congestive cardiac failure
25	71	F	140/60	350	L D , R	L V A , L V P	L V A , L V P	Syncope
29	43	M	172/120	480	L D , L C	L V A	L V A , O M	Syncope
30	53	M	150/110	535	L D , L C	L V A , O M		Syncope
37	60	M	184/80	590	R	L V A	L V P	Congestive cardiac failure
40	47	M	120/80	580	L D , L C	L V A , L V P	L V P	Lung abscess
42	61	M	220/140	425			L V A	Syncope
46	55	M	190/100	400	L D , R	L V A	L V P	Hæmopericardium
51	65	M	95/60	495	R		L V P , R V P	Sepsis
52	53	M	120/80	480	L D , L C	L V A	L V A , L V P	Congestive cardiac failure
55	71	F	175/105	630	L D , R		L V P	Congestive cardiac failure
66	69	M	140/80	656	L C , R	O M	L V P , R V P	Myocardial infarction
70	63	M	140/105	480	L C , R	L V P	L V P	Myocardial infarction
73	64	F	180/110	505	L D , L C , R	L V P , L V A	L V A , L V P	Congestive cardiac failure

* L D = Left descending branch   L C = Left circumflex branch   R = Right coronary
† L V A = Left ventricle anterior   L V P = Left ventricle posterior   R V P = Right ventricle posterior   O M = Obtuse margin   I V S = Interventricular septum

is 90 g and the standard error of the difference is 9 7 g This correlation between duration of failure and heart weight is similar to our finding in the hypertensive group, and is further evidence that cardiac failure is an important factor in the production of myocardial hypertrophy

Coronary arteries The skiagrams (Fig 6) and cleared specimens (Fig 9 and 10) of the injected coronary vessels in the ischæmic cases showed a characteristic picture, quite different from that of the hypertensive group The characteristic feature was the constant presence of severe narrowing or occlusion, usually both There was, of course, some variation in the degree and extent of the lesions In eight cases the whole coronary tree was affected and all the major arteries were narrowed and irregular in outline, often with deposits of calcium salts in their walls Complete occlusions in both right and left coronary arteries were usually demonstrable

In the other seven cases arterial narrowing was limited either to one vessel (usually the left) or to part of a vessel, whilst the rest of the coronary tree was relatively normal In some of these cases the unaffected vessels were wider than *normal* The mean heart weight was slightly higher (527 g) in cases with localized coronary narrowing than in those with generalized coronary narrowing (460 g) Out of four with no history of angina of effort (Cases 17, 30, 40, and 51), three were examples of localized coronary narrowing

Coronary occlusion was commonly multiple as previously indicated, though in one case it was incomplete, and in four it was single, there were eight cases with two blocks and two cases with three blocks The distribution was as follows out of twenty-six complete occlusions eighteen were in the left coronary artery and eight in the right Myocardial infarction was found in thirteen out of fourteen cases with one or more complete occlusions The case without complete occlusion had no infarct but only microscopic foci of necrosis The other (Case 37) without infarction had a solitary occlusion of the right coronary artery, and showed only microscopic necrosis Amongst the other thirteen cases there were fourteen healed infarcts and eleven recent infarcts, all but one involving the left ventricle The areas affected were the apex anteriorly (11 cases), the base posteriorly (10 cases), the obtuse margin (3 cases) and the base of the right ventricle posteriorly (1 case) In each of these twenty-five infarcts the appropriate coronary artery was completely occluded There was no correlation between the type of lesion present and the mode of death Syncopal deaths were not particularly associated with recent thrombi or infarcts

Anastomotic vessels, just big enough to be visible in the skiagrams, were noted in all cases These occurred in relation to the distal parts of occluded vessels, and sufficed to permit retrograde filling of these vessels They were better seen in the " cleared " specimens (Fig 9 and 10)

Histology Coronary vessels With certain reservations histological study of the coronary

arteries confirmed the radiographic findings In most of the skiagrams, however, no matter how irregular or narrowed the majority of the vascular lumina, some segments still looked normal both in calibre and in smoothness of outline, yet microscopically these parts also showed severe atheroma A similar discrepancy was observed both in the controls and in the hypertensive cases, but it is

repeated for emphasis that even in manifest ischæmic heart disease, the appearance of atheroma in a section of a coronary artery does not necessarily indicate narrowing *in vivo* at that site Again, it was quite impossible to tell from the skiagrams whether a focus of narrowing was due to atheroma or to a recanalized thrombus On numerous occasions points of narrowing noted in the skia

FIG 9 —Ischæmic heart   Case 46   Anterior view showing small coronary arteries with irregular outlines, complete occlusion in right coronary artery, and anastomoses via pericardial vessels

grams and in cleared specimens proved to be healed thromboses in which the recanalized lumen was as large as the adjacent narrowed atheromatous vessel This may explain the occurrence of myocardial infarction in the presence of patent, though narrowed, vessels, for the absence of complete occlusion at autopsy does not prove the vessel was never blocked during life These examples of organized recanalized thrombi were ones in which the histological diagnosis was unequivocal but apart from these there were many others in which such an interpretation would be difficult to refute In late cases of recanalized thrombosis, the fibrous tissue replacing the thrombus fuses with atheromatous lesions so intimately that we were often unable to tell whether a given lesion was atheromatous or thrombotic This difficulty was accentuated when atheromatous lesions showed undue vascularity of hæmorrhage as described by Winternitz *et al* (1938) Both phenomena were observed in some sections of the coronary arteries in nearly every case When the vasa vasorum were small the hæmorrhages were fresh, it seemed fair to assume that they were late effects of atheroma but when the vasa were large and ran parallel with the coronary artery, and when blood in the plaque was represented only by groups

FIG 10 —Ischæmic heart Case 25 Showing recanalized occlusion of the descending left coronary artery and irregularity of outline in others
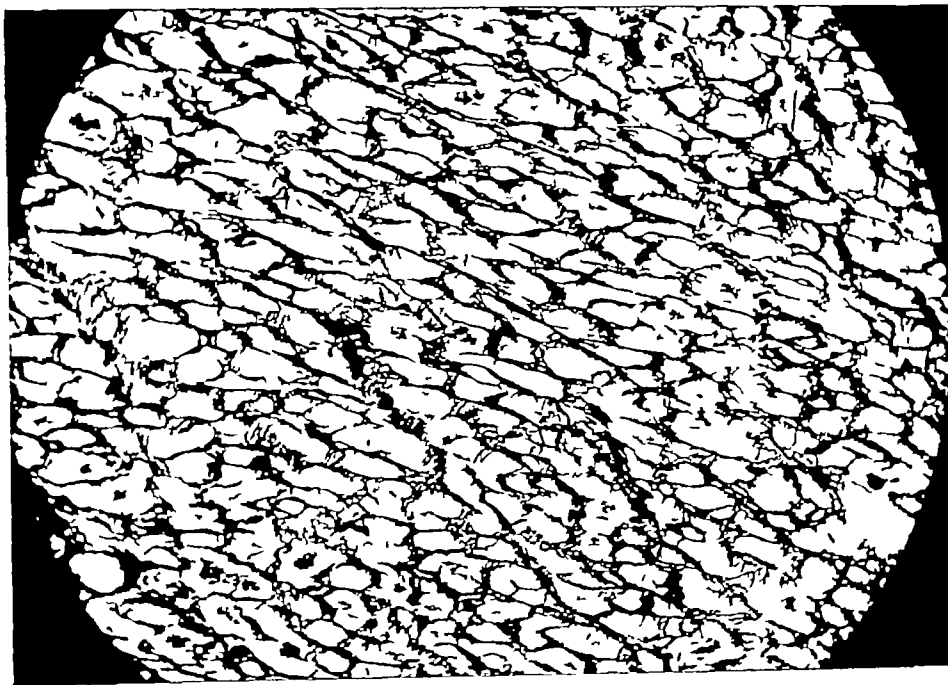
A

B

FIG 11 —Section of heart muscle   (A) *Hypertensive heart disease* (*Case* 11), and (B) *Control* (both magnified ×108) showing hypertrophy of interstitial connective tissue in myocardial hypertrophy reticular fibrosis "   Silver impregnation

of macrophages filled with pigment it became impossible to decide whether or not there had been thrombosis This similarity lends support to the hypothesis recently put forward by Duguid (1946) that what is ordinarily regarded as coronary atheroma is, in fact, the result of organized thrombi

Myocardium The histological appearances of the myocardium in the present series of cases conformed to the accepted descriptions of ischæmic heart disease, but there were two points that merit some discussion The first is the time relation between coronary closure and myocardial infarction In the majority of cases these corresponded Recent infarcts were associated with recent thrombi and old infarcts with old thrombi Furthermore, they were associated in position, the infarcts occurring in sites supplied by occluded vessels We did not observe any cases in which infarction was due to the closure of a vessel supplying the infarcted area only by anastomoses, though this has been observed by Blumgart *et al* (1940) We did, however, observe three examples (Cases 29, 46, and 55) in which recent infarction was unassociated with recent thrombosis in any vessel big enough to be visible macroscopically In two of these (Cases 29 and 46) the symptoms of the fatal infarct arose at home whilst the patient was at rest, and the lesion cannot therefore be attributed to unusual circulatory demands beyond the capacity of the coronary supply It is possible that a period of diminished cardiac output may have reduced the coronary flow sufficiently to have precipitated the infarcts, but there was no evidence available on this point Coronary spasm can almost certainly be excluded on the grounds that the coronary tree was too rigid for this to be possible These cases are of importance because they may represent the late counterpart of cases of sudden death in ischæmic heart disease where neither recent occlusion nor fresh infarction is demonstrable at autopsy It is possible that such cases, which are common in forensic practice, might show infarction if they survived long enough

The second feature noted in the present series was the development of minute foci of necrosis leading to focal fibrosis These small lesions, usually just visible macroscopically, were encountered in ten of the sixteen cases, often in several sites in one heart We were able to observe every stage of their development, and they showed exactly the same changes as do ordinary infarcts, but on a minute scale It appears to us desirable that these lesions should be regarded as minute infarcts, and that the term ischæmic fibrosis should imply this In most cases these small lesions were found to be related, both in time and site, to occluded coronary branches, but

this was not always so Minute infarcts without demonstrable vascular occlusion presumably have the same pathogenesis as their larger counterparts

DISCUSSION

Previous history The high incidence of a history of rheumatic fever in both hypertensive and ischæmic groups is regarded as coincidental for necropsy revealed evidence of rheumatic heart disease in but one case and the known facts deny relationship Thus, of 542 cases with granular kidney reported by Pitt (1887), 6 per cent had mitral stenosis Of 403 clinical hypertensives analysed by Boas and Fineberg (1926), 8 per cent had mitral stenosis Of 1000 hypertensive cases studied by Bechgaard (1946) 1 per cent had clinical evidence of mitral stenosis Finally, in 122 hypertensive subjects under 50 years of age, Haloven and Salomaa (1947) found a history of rheumatic fever in 6 6 per cent, compared with an incidence of 9 8 per cent in 250 controls Although figures from the paper by Pitt and by Boas and Fineberg, and also those given by Levine and Fulton (1928) show that about 40 per cent of cases of mitral stenosis have hypertension, it must be remembered that 33 per cent of men aged 40, and 43 per cent of women aged 40, have a blood pressure of 150/100 or above (Master *et al*, 1943) Claims that the rheumatic process may involve the coronary vessels (Plesch, 1947) cannot be denied, but there is no statistical evidence implicating rheumatic fever as an important etiological or contributory agent in the development of the common form of ischæmic heart disease

Family history Platt's suggestion that essential hypertension may be a hereditary disease transmitted as a Mendelian dominant with a rate of expression of over 90 per cent (Platt, 1947) cannot be easily dismissed Thus it may be calculated from Berchgaard's findings in over 1000 hypertensive subjects that the incidence of high blood pressure in the parents was about 75 per cent (Bechgaard, 1946), and the author considered that about 20 per cent of his cases were renal in origin—a group in which the hereditary factor has been shown to play no part

The hereditary aspect of ischæmic heart disease has been less frequently studied, and has been rarely separated from the hypertensive group General opinion, however, strongly favours hereditary predisposition

Age and sex Our figures bear out the well-known difference in sex and age incidence The ratio of males to females is usually given as about 4 1 in ischæmic heart disease, whereas it is close to 1 1 in essential hypertension It is also recognized that the preponderance of males in ischæmic

heart disease is proportional to the age of the groups studied   Thus it is overwhelming in those under 40, 8 to 1 in those between 40 and 49, 4 to 1 in those between 50 and 59, 2 to 1 in those between 60 and 69, and the sex ratio is equal in those over 70 (Hedley, 1939, Gordon *et al*, 1939)

Clinical features   The steady downhill course of hypertensive heart disease was well illustrated, and contrasted sharply with good temporary recovery in at least one-third of the ischæmic cases   This latter behaviour may be attributable to coronary thrombosis with or without infarction, followed by improvement in the collateral coronary circulation

More than half the hypertensive group died from non-cardiac causes, chiefly uræmia or cerebral hæmorrhage   Only two died suddenly   On the other hand, ten out of fifteen ischæmic cases died abruptly   This confirms the well-known fact that ischæmic hearts are peculiarly liable to develop ventricular fibrillation, but it also demonstrates that hypertensive hearts are not

Of great interest was the rarity with which cases initially classified as hypertensive later developed angina pectoris or myocardial infarction   The pathological studies provide a ready explanation for this, for they show that the typical hypertensive heart has smooth distended coronary arteries   It is not denied that about 66 per cent of ischæmic cases have a blood pressure over 150/90, (Master *et al*, 1936), or that nearly 50 per cent have a blood pressure at least 160/100 (Riseman and Brown, 1937), but we agree with the latter authors that systolic pressures over 200 are rare   It must be repeatedly pointed out that about half of the population between the ages of 50 and 60 have blood pressures of 150/100 or above (Master *et al*, 1943), and it is therefore misleading to quote similar figures in ischæmic heart disease, which involves particularly this age-group, as evidence that coronary disease is intimately related to hypertension   The difference in the quality of the cardiac impulse in the two groups and in the size of the heart as viewed fluorscopically, was most impressive

The pathological findings proved conclusively that the hypertensive electrocardiographic pattern showing left axis deviation with depression of the RS–T segment with or without inversion of the T wave in lead I was not due to coincident coronary disease nor to myocardial fibrosis, but appeared to closely related to the size of the left ventricle   Likewise, auricular fibrillation and bundle-branch-block occurring in hypertensive heart disease could not be ascribed to ischæmic fibrosis   Admittedly, bundle-branch-block was twice as common in ischæmic as in hypertensive heart disease in the

clinical series, occurring in 10 per cent and 20 per cent of the cases respectively

PATHOLOGICAL FEATURES

The most striking observation in the injected hearts was the basic difference in the coronary pattern between the hypertensive and ischæmic series and the lack of overlap between them   It is probably true that hypertension does predipose to coronary sclerosis, but our findings suggest that the relationship has been overstressed   Confusion may have arisen on account of the frequency at autopsy of enlarged hearts with atheromatous coronary arteries—it being assumed that the hypertrophy indicates previous hypertension and atheromatous coronary arteries indicate ischæmia   Either of these assumptions may be false   Our observations show that in coronary sclerosis cardiac failure can produce myocardial hypertrophy to an average weight of 550 g irrespective of a raised blood pressure   This has been observed by Bartels and Smith (1932) and by Davis and Blumgart (1937), and Eyster (1927, 1928) has suggested that stretching of the heart by dilatation is the essential stimulus to hypertrophy   In spite of this, the assumption is still commonly made that a heart weight of over 500 g indicates hypertension   Another source of error is the assumption that atherosclerosis must cause coronary narrowing   Stewart *et al* (1935) showed that this was not so and our present findings confirm this   It is not suggested that atheroma does not lead to ischæmia but we believe that by ordinary examination it is very difficult to estimate whether or not the vessels are narrowed during life

Our observation that the coronary arteries enlarge as the heart hypertrophies confirms the previous findings of Gross (1921), Russow (1936), Fishberg (1937) and Sagebial (1934), but in addition they strongly suggest that the degree of coronary enlargement keeps pace with the needs of the heart and that " relative " ischæmia is not a cause of cardiac failure in hypertension   The concept of relative ischæmia has probably arisen from the finding of myocardial fibrosis unassociated with appreciable coronary sclerosis   Such fibrosis may be of the type which we have called reticular and which we believe to be a form of fibrous tissue hypertrophy and not an indication of muscle destruction   This was also the view of Stadler (1907)   Alternatively, there are undoubtedly cases of focal myocardial fibrosis indistinguishable from healed infarcts but unassociated with any coronary occlusion   Such cases have been observed by Blumgart (1940, 1941), Gross and Sternberg (1939), Ravin and Greeves (1946) and by Holyoke (1945), as well as by us   We suggest that it is more reasonable to attribute them to a diminu

tion of coronary flow during a phase of cardiac failure than to postulate either relatively small coronary arteries or spasm

SUMMARY AND CONCLUSIONS

Comparative clinical and pathological studies have been made on twenty-seven cases of hypertensive heart disease and fifteen cases of ischæmic heart disease There were twelve controls

Hypertensive cases were characterized clinically by even sex distribution dyspnœa, steady deterioration, retinopathy, cerebral symptoms impairment of renal function, anæmia, auricular fibrillation and by clinical, radiological, and cardiographic evidence of left ventricular enlargement before the onset of heart failure Only one case originally classified as hypertensive developed subsequent angina pectoris or myocardial infarction Death was rarely abrupt

Ischæmic cases were characterized clinically by an unequal sex distribution favouring men, the older age of women, the infrequency of early dyspnœa, the absence of anæmia, of retinopathy and of cerebral symptoms, good renal function normal rhythm, normal heart size before failure, good temporary recovery, and by abrupt death

At autopsy the hearts were investigated by injection of the coronary arteries followed by stereoscopic radiography and dissection and histological examination The following conclusions were drawn

Moderate degrees of coronary atheroma do not necessarily cause narrowing

The size of the coronary arteries varies directly with the heart weight in both normal and hypertrophied hearts irrespective of the cause of the hypertrophy

The coronary arteries vary sharply between hypertensive and ischæmic cases in the former they are large with smooth bores, in the latter they are narrow and frequently occluded

In hypertensive cases the heart weight varies with the degree of failure during life and not with the height of the blood pressure

The coronary size increases as the heart size increases and there is no evidence to indicate relative ischæmia of the ventricular muscle

In severely hypertrophied hearts the normal fibrous tissue increases in thickness

In ischæmic cases cardiac hypertrophy is the rule and can be correlated with the duration of failure

Myocardial infarction can occur in the apparent absence of coronary occlusion and is probably then due to circulatory failure

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SINO-AURICULAR BLOCK, INTERFERENCE DISSOCIATION, AND DIFFERENT RECOVERY RATES OF EXCITATION IN THE BUNDLE BRANCHES

BY

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Disturbances in the propagation of the heart beat between the auricle and the two ventricles are of frequent occurrence and well known under the terms A-V dissociation or heart block The term sino-auricular block is the standard name for an apparent block between the sinus node and the auricle, a hypothetical incident to explain transient auricular standstill for a period of time that is a multiple of the length of the regular sinus cycle Interference dissociation is commonly associated with a nodal rhythm with retrograde block, the slower sinus excitation and auricular beat being conducted intermittently to the ventricle Less commonly, interference dissociation is seen in cases of near complete A-V dissociation, with occasional sinus beats being conducted in a favourable time period, a phenomenon usually attributed to the likelihood that junctional tissues have a supernormal phase of excitation and conductivity following their refractory period Some of the best examples of this phenomenon are the first case of Lewis and Master (1924), the cases of Wolferth (1928), of Luten and Pope (1930), of Pareja (1933), and the first case of Burchell (1942)

Electrocardiographic records obtained recently from a woman, aged 60, exhibited the recurring phenomenon of nodal rhythm with interference dissociation in which the ventricular beat conducted from the auricle showed the presence of either left or right bundle branch block The unique feature was the fact that the type of bundle branch block exhibited was determined by the time relationship between the P wave that was to be followed by a ventricular response and the preceding R wave of the idioventricular (nodal) beat The explanation seemed related to either different rates of recovery in conduction in the two bundle branches or a supernormal phase either of conduction in the left bundle

or of excitation in the left ventricle As there were, in addition, frequent cardiographic sequences showing the picture of sino-auricular block, the possible relationship of this abnormality to the disturbance in A-V and intraventricular conduction invited some speculation

REPORT OF CASE

A woman, 60 years of age, registered at the clinic with the main complaints of varicose veins, painful feet related to corns, mild shortness of breath, slight substernal discomfort with moderate exertion, and backache No history was elicited that digitalis or other medicines had been taken Auscultation of the heart revealed no murmurs The blood pressure was 140 systolic and 90 diastolic There were extensive varicosities of the veins of both legs and a stasis ulcer on the lower part of the left leg The roentgenogram of the thorax showed moderate generalized cardiac enlargement The roentgenogram of the spinal column showed a dorsal kyphosis and moderate osteo-arthritic changes The cardiac diagnosis was coronary sclerosis and angina pectoris

Electrocardiographic study On the short cardiographic sequences obtained for routine evaluation there was noted an intermittent type of A-V dissociation during which occasional A-V conduction occurred Only a few such complexes were present and the initial cardiographic diagnosis was probable A-V dissociation with interference dissociation, the occasional conduction being related to a supernormal phase of conduction The patient returned the following day for more extensive study For about the first fifteen minutes of electrocardiographic sampling, normal sinus rhythm was present and this was not affected by pressure on either carotid sinus Then spontaneously a cardiac irregularity appeared

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and a continuous record was obtained for approximately three minutes, during which about twenty-five premature beats were noted The developed records showed phenomena similar to those of the preceding day but the abnormal mechanisms could be more definitely interpreted

The various disturbances in rhythm and conduction are illustrated in Fig 1 and 2 In Fig 1, there are shown in the four tracings from above downward respectively, first, normal sinus rhythm with slight sinus arrhythmia, the P-P intervals

In Fig 2, the top sequence shows the usual or classic picture of interference dissociation in which the nodal rhythmicity rate is faster than the sinus rate, and a retrograde block is present The R-R intervals of the nodal rhythm measure 1 68 sec and the P-P intervals of sinus rhythm 1 76 sec , thus the record shows that the P waves gradually appear later and later after the R wave until finally the junctional tissues are found non-refractory and an interference beat occurs, and in the record portrayed there is an associated prolonged P-R interval
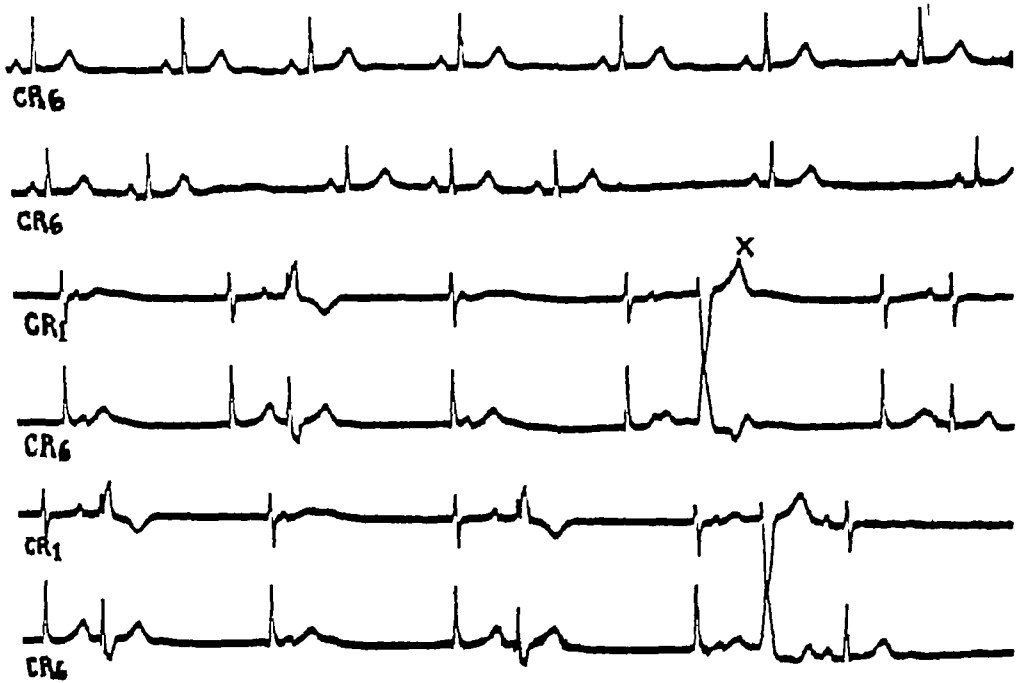

FIG 1 —Electrocardiograms discussed in the text Four sequences are shown In the lower two pairs of records, simultaneous tracings from two præcordial positions are shown, position 1 being in the fourth interspace just to the right of the sternum and position 6 being in the fifth interspace in the left midaxillary line The indifferent electrode was on the right arm

varying from 1 24 to 1 56 sec , second, sequences of S-A block, the heart being more rapid and the regular P-P intervals showing only slight variation and averaging 0 96 sec , and third and fourth, nodal rhythm with interference dissociation in the simultaneously taken right and left præcordial leads The third tracing shows three premature ventricular beats, the first having the complex of right bundle branch block, the second that of left branch block, and the third a normal QRS complex The fourth tracing shows two premature right bundle branch complexes and one left, the latter being interpolated between two normal QRS complexes

and left bundle branch block In the lower tracing of Fig 2 are shown three premature beats, the first with a left bundle branch block complex, the second with a normal QRS complex, and the third with a right bundle branch block, and then return of normal sinus rhythm It is to be noted that the premature ventricular beats have a definite time relationship to a preceding P wave and, depending upon the interval between the P wave that is to be followed by conduction and the preceding R wave of the nodal beat, the ventricular complex will show left bundle branch block, right bundle branch block, or a normal QRS complex

Particular attention needs to be paid to the left bundle branch block complexes in the third tracing in Fig 1 and in the bottom tracing of Fig 2 where the T wave is deformed (marked X) by an apparent P wave of abnormal shape   These P waves occurred commonly after the left bundle branch block complexes but never with the right bundle branch block complexes   While these P waves possibly are indicative of auricular extrasystoles, the constant association with the left bundle branch complexes and the preceding prolonged P–R interval suggest that such P waves represent a re-entry into the auricle, in fact indicating auricular reciprocal beating

COMMENT

The acceptance of the concept of a sino-auricular block is dependent only on the evidence of sudden

excitation could not be readily measured   The frequent close association of a P wave with the R wave when a supposed nodal rhythm was present might theoretically be related to sino-ventricular conduction and partial sino auricular block   The progressive increase in the R–P times in the sequence shown in Fig 2 could be related to a progressive increase in S–A conduction time   The conducted beat of the interference dissociation sequence, if such premises were accepted, could then represent reciprocal rhythm   While a progressive increase in S–A time or a Wenckebach phenomenon has been claimed, on good evidence (Decherd *et al*, 1946), to occur, it is most unlikely that the phenomenon of sino-ventricular conduction without auricular response would have occurred without many examples of dropped auricular beats having been observed   Orthodox views, however, regarding the
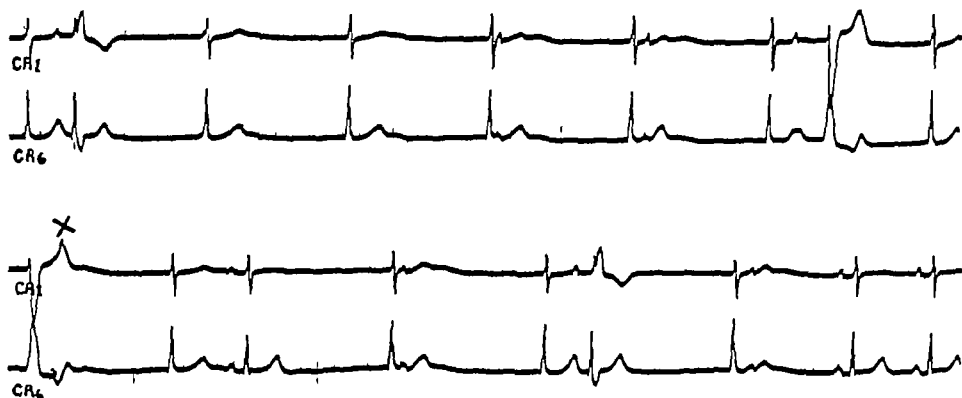

FIG 2 —Electrocardiograms discussed in the text   Two pairs of records with simultaneously recorded præcordial potentials are shown

halving of the auricular rate, and all the objections of Lewis (1925) to the term and its implications still pertain   In the case reported herein, the disturbance in sinus rhythm resulting in marked auricular slowing allowed a lower rhythm centre to drive the ventricle and permitted the development of circumstances that give the picture of interference dissociation   If there were specialized conducting pathways between the sinus node and the A-V node, as Eyster and Meek (1914 and 1922) interpreted their experiments to indicate, and if one were to assume the presence of an entrance block into the auricle, a curious phenomenon of a sino-ventricular beat without an auricular contraction could occur   As Lewis *et al* (1914) incidentally noted in their criticism of Eyster and Meek's investigations, excitation potentials related to sino-auricula-ventricular nodal conduction without contingent auricular

nature of nodal rhythm with and without retrograde conduction to the auricle would seem to be well agreed upon, and they are explained and illustrated in standard textbooks on electrocardiography   The relatively short intervals in ventriculo-auricular and auriculo-ventricular sequential beats during heart block has probably attracted the attention of many investigators, and the problem was reviewed by Wolferth and McMillan (1929) who emphasized that the auricular elements of the sequences were represented by abnormally shaped and usually inverted P waves   The possible auricular re-entry beats in this case (Fig 1 and 2) associated with conduction defects in the main bundle and left bundle block complexes are particularly interesting in that there was never retrograde conduction to the auricle during the long sequences of nodal rhythm

The only published electrocardiographic records seen that approach the nature of the tracings in the case reported herein are those shown in Fig 196 of Scherf and Boyd's *Clinical Electrocardiography* (1946) The tracing is interpreted as showing extreme sinus bradycardia through 2 1 sinus block with escaped beats and interference dissociation with the conducted sinus beats showing an aberrant QRS complex owing to abnormal spread within the ventricle The tracings demonstrating interference

except for one conducted beat where there is impaired bundle branch conduction

In the present case the number of observations seems sufficient to establish evidence of an absolute pattern of conduction in the main bundle and bundle branches dependent upon the time the P wave came after the R wave of the preceding nodal beat The switch from left bundle branch block to right bundle branch block occurred at a critical time interval and was associated with a sharp decline in total A-V
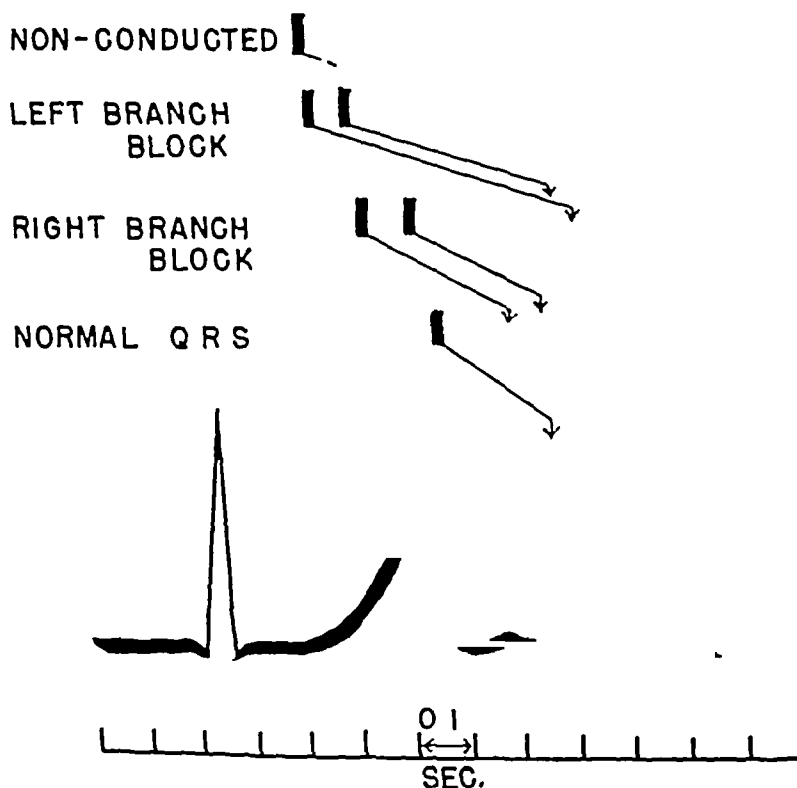

FIG 3—The diagrammatic illustration shows the relationship of P waves, represented by the black rectangles, to the preceding R wave of the nodal beat in respect to whether they are followed by left or right branch block complexes or a normal QRS complex See text for explanation

dissociation published by Jervell (1934) show complexes of the bundle branch form, but in these tracings nearly normal QRS complexes may occur with the same R–P and P–R intervals as those in which the intraventricular conduction defect is present

The case in the paper by Cowan (1939) may have been similar to that of the case reported herein in that the records were said to show " variable sino-auricular block, the auricular rhythm being very irregular and infrequent " One tracing that was reproduced shows complete A-V dissociation

conduction (Fig 3) With the sequences showing left branch block there was a definite tendency for the total A-V conduction time to be shorter as the P wave fell farther away from the preceding nodal complex, but with the right bundle block complexes the total A-V conduction time remained relatively constant (Fig 4)

One of the main difficulties in appraising the nature of the conduction of the interference beat is the lack of knowledge of the exact origin of the nodal beat within the junctional tissues If such know-

ledge were available the refractoriness of the upper and lower portions of the junctional tissues relative to one another might have been better estimated The difficulties of interpreting the effects of blocked retrograde impulses on the refractoriness and possible supernormal phases of junctional tissues and myocardium have been emphasized by Langendorf (1948) and Mack *et al* (1947)

One explanation of the phenomenon of the rapid alternation in the type of bundle branch block is illustrated in Fig 5 It is assumed that the nodal beat originated in the upper portion of the junctional tissues so that the main bundle precedes that of the bundle branches in phases of excitation and refractoriness The earliest P waves followed by conduction are shown to occur in the partially refractory state of the main bundle, and when the excitatory process reaches the bundle branches, the left

bundle branch is completely refractory and the right partially refractory Left branch block associated with partial right branch block is then present The term ' partial right branch block " is used as an equivalent to the term " partial heart block " when the latter means an abnormal prolongation of the P–R interval

The diagram (Fig 5) shows rapid recovery in the left branch so that an excitatory process traversing the main bundle at a later period travels more quickly through the left branch than through the right and a right branch block is manifest A supernormal phase of conduction in the left branch might be added to the basis for the explanation but seems unnecessary If the diagram as drawn were truly representative of the conditions, there would be a partial left branch block in addition to a manifest right branch block
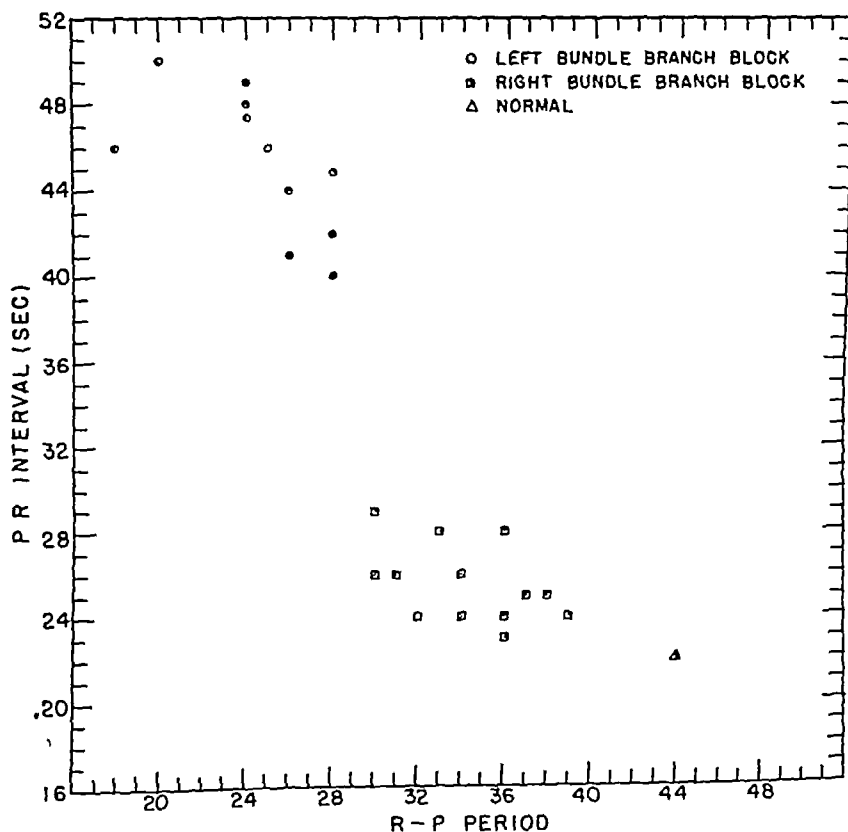

FIG 4 —A graph to illustrate the relationship between the R–P period (the time interval between the beginning of the P wave that is to be followed by a ventricular complex and the preceding R wave of the nodal beat) and the P–R interval (the A–V conduction time) The sharp reduction in total A–V conduction when left branch block is replaced by right branch block is clearly shown

HYPOTHETICAL RECOVERY CURVES OF
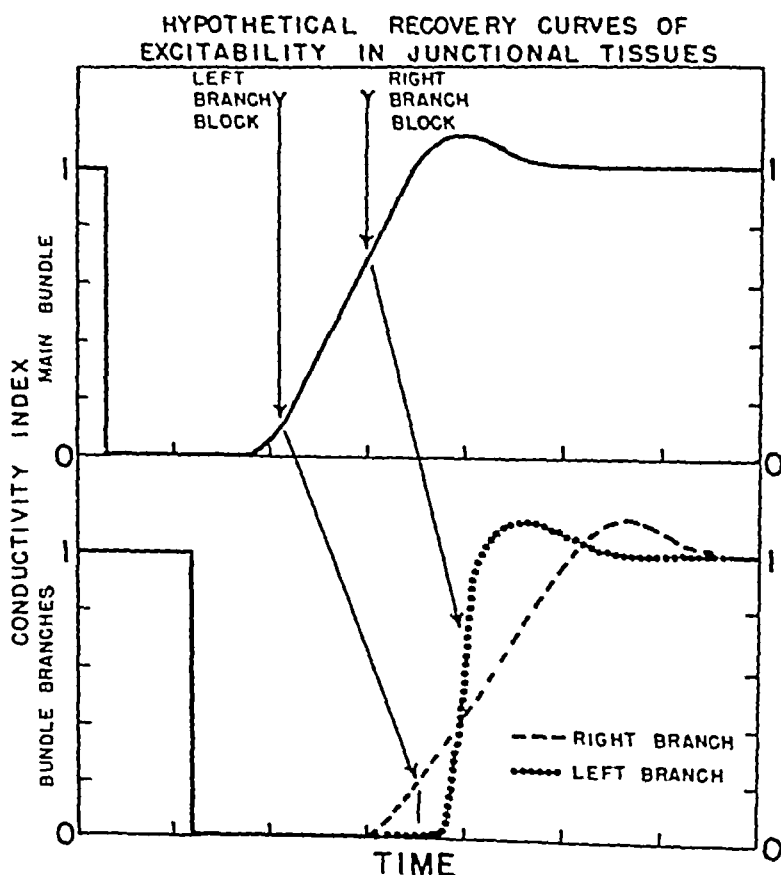## EXCITABILITY IN JUNCTIONAL TISSUES

FIG 5 —The diagram illustrates hypothetical recovery of excitation curves or periods of total and partial refractoriness, of junctional tissues The conductivity index represents variations in refractoriness, O being total refractoriness and 1 being normal conductivity The interpretation as applied to the case reported is discussed in the text

The term " partial branch block ' is somewhat confusing because the complete cardiographic record obtained will be dependent upon conduction in both bundle branches For example, if the left bundle branch is normal, then depressed conduction in the affected right bundle branch gives rise to the picture of various degrees of incomplete right bundle branch block as originally discussed from the experimental and clinical cardiographic viewpoints by Wilson and Herrmann (1920) If both the bundle branches have similarly depressed zones of conductivity, the P–R interval is prolonged and the QRS complex is of normal duration If there is complete loss of conductivity in one bundle branch, for instance, the left, and depressed conduction in the other, the right, then as happened in the case reported herein, there is an increased P–R interval and complete left branch block

Excellent illustrations of bilateral branch block have been published by Bain (1941), Case 3 in his article being of particular interest Incomplete heart block is shown, the usual mechanism being a 2 1 heart block with right branch block, but occasionally two auricular beats are conducted in sequence, the second of which shows a prolonged P–R interval and a left, rather than a right, branch block It seems reasonable to suppose in Bain s case that retarded conduction was present constantly in the right bundle branch, and when the left bundle branch conducted normally, right bundle branch block was manifest However, when the left bundle branch was completely blocked, the right bundle branch conducted after a delay, resulting in an increased P–R interval and left branch block

In the case reported herein it would seem a

justifiable assumption that the depressed zones of conduction in the bundle branches were associated with a pathological state in the upper part of the ventricular septum   Utilizing the conception of unidirectional block related to the orientation of slightly depressed to severely depressed zones in the bundles, as outlined by Herrmann and Ashman (1931), one might explain the observed conduction defects in the following way   The first excitatory processes to be conducted meet a severely depressed area in the right bundle branch which, however, is eventually traversed, while in the left bundle branch there is a slightly depressed zone above a severely depressed area and complete block in the left bundle branch occurs   A tenth of a second or so later, the left bundle branch has recovered, the excitatory process passes quickly through it, and a right bundle block complex appears   In general, it would appear that the right bundle branch conduction defect simulates type 1 A-V block while the left bundle branch conduction defect simulates type 2 A-V block as classified by Mobitz (1928), type 1 being a progressive increase in conduction time culminating in complete block, and type 2 being the sudden appearance of complete block without preceding increase in conduction time

The possible relationship of the conduction disturbances to the clinical diagnosis of coronary insufficiency may be allowed if it be accepted that the blood supply to the conducting tissues were jeopardized   When normal sinus rhythm was present, there was never any auriculo-ventricular or intraventricular conduction defect   One might presume on a theoretical basis a further phasic decrease in blood supply during ventricular systole during which period the P wave that was to be followed by the bundle branch block QRS occurred Such a supposition concerning the effect of systole on the blood supply to an ischæmic zone is the direct opposite to that proposed by Wolferth (1928) in explaining the A-V conduction in his case   If the phenomena observed were the effect of anoxæmic anoxia, the question of a possible elucidation of the problem from the work of Harris and Matlock (1947) arises   These investigators reported that the threshold of excitability was lowered and conduction rates increased in moderate anoxia while in severe anoxia the reverse effect was obtained   If the results were applicable to junctional tissues, one might explain the phenomenon of the sudden increase in conductivity and perhaps even an increase of excitability in the left ventricle in this case by assuming that a hypoxic environment changed from a severe state to a moderate one

SUMMARY

A patient having intermittent sino auricular block and interference dissociation was found to have also bundle branch block associated with the majority of the interference beats   The bundle branch block was either right or left, dependent upon the time relationships of the auricular beat to be conducted and the preceding R wave of the nodal (idioventricular) rhythm   The possibility of an intraventricular supernormal phase of recovery in conductivity in the left bundle branch might be utilized in explaining the phenomena, but it is not necessary if different recovery rates in excitation of the two bundle branches are hypothesized

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ELECTROCARDIOGRAPHIC STUDIES IN CRETINS

BY

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There is no direct method of estimating accurately the function of the thyroid gland so other measures have to be employed in diagnosing thyroid deficiency and in regulating subsequent treatment Recognition of typical cases of hypothyroidism should not be difficult, but there are borderline cases with slight symptoms that are not so easy to detect Standard methods of investigation are helpful but have their limitations particularly in young children At this early age, for instance, accurate estimation of the basal metabolic rate is difficult and therefore unreliable The blood cholestrol level is usually raised in hypothyroidism, but the test may fail in early or mild forms of the disorder and other conditions may be associated with a high figure

In searching for additional means of diagnosis attention has been drawn to certain electrocardiographic changes pointing to a disturbed action of the heart This method of investigation has been used only to a very limited extent in children and pædiatric textbooks contain little or no information on the subject

ELECTROCARDIOGRAMS IN HYPOTHYROIDISM

In 1918 Zondek described cardiac disturbances in four adults suffering from hypothyroidism and on the basis of his observations introduced the term "myxœdema heart" The main changes he described were cardiac dilatation, a depressed heart action with a slow pulse rate but normal blood pressure, and the absence of the P and T waves in the cardiogram After thyroid treatment all these abnormalities disappeared Since then cardiographic investigations of this condition have continued, mostly in myxœdematous adults, but there have also been a few sparse references to children (Cori, 1921, Nobel et al, 1924, Thacher, 1924, Doxiades and Pototzky, 1927, Fournier, 1942, and Sharpey Shafer, 1943)

The changes generally reported are a low voltage curve with flat P and flat or negative T waves Only

two references can be found to alterations in the R-T segments Chini (1929) reported two myxœdematous children in whom the segment had a convexity, 'a tipo coronarico' similar to Pardee's original description in coronary sclerosis Ohler and Abramson (1934) found similar changes in 4 of 21 adults with hypothyroidism Prolongation of the P-R interval has been observed in isolated cases (Luten 1920 Schittenhelm and Eisler 1927, Ziskin, 1930 Davis 1931 and Howard 1929) and a lengthening of the QRS complex in others (Holzman 1929)

Arrhythmias associated with myxœdema seem to be extremely rare Solitary cases of auricular fibrillation and occasional premature contractions have been described (Ohler and Abramson 1934, Guerrant and Wood, 1938, Willius and Haines, 1925, Walker, 1933, and Austin, 1937) Bradycardia of sinus origin or with complete heart block and the Stokes-Adams syndrome is sometimes encountered (Willius, 1925) Paroxysmal tachycardia is rarer still (Lisser and Anderson, 1931)

There is a general impression that abnormal electrocardiographic changes in myxœdema disappear in the majority of cases after some weeks thyroid treatment Flattening of the P and T waves has been noticed after thyroidectomy designed to produce artificial myxœdema in the treatment of congestive heart failure and angina pectoris (Davis et al, 1934) or when thyroidectomy has been carried out too liberally for Graves disease (Hamburger et al, 1929) Animal experiments in support of this have not, however, produced constant results (Burlage, 1922, Coelho, 1931, and Lueg, 1926)

THE CAUSE OF ELECTROCARDIOGRAPHIC CHANGES IN MYXŒDEMA

Various explanations have been given of the cause of these changes An extra-cardial factor such as increased skin resistance has been one popular theory, but there is an increasing belief that an

alteration in the heart and the conductive mechanism as a result of the hypothyroid state is primarily responsible

Cutaneous resistance In order to overcome the possible effect of skin changes in myxœdema, Nobel *et al* (1924) used subcutaneous needle electrodes and found an increase in the height of the P and T waves compared to the tracing obtained with ordinary standard leads From this they concluded that the skin and not the heart was primarily at fault

Other investigators have not been able to confirm these observations and, furthermore, alteration of skin conductivity could hardly account for the prolonged conduction time and other abnormalities observed The absence of cardiographic changes in skin diseases with extensive cutaneous thickening such as scleroderma and ichthyosis is also of some significance (Hallock, 1934) This has also been our experience in these disorders, in dermatomyositis, and with the widespread œdema of nephrosis

Sherf and Boyd (1945) using a special electrocardiograph were able to measure the electrical potential directly from the heart In myxœdema abnormally low potentials were recorded, indicating a lesion of the heart itself

Pericardial effusion Some authorities have attributed the cardiographic changes to a pericardial effusion which may arise in myxœdema With thyroid treatment the accumulated fluid disappears and the cardiogram becomes normal, which might be advanced as further proof of the argument (Schnitzer and Gutmann, 1946) But on the whole these effusions are not common and we have never observed them in any child suffering from hypothyroidism

Nervous factors A decreased tone of the autonomic nervous system might influence the deflexions, especially of the T wave, but here again it hardly seems likely that this factor alone could produce the various other abnormalities (Hamburger *et al*, 1929, Ohler and Abramson, 1934, v Pfaundler, 1938)

Anæmia Secondary anæmia, nearly always present in myxœdema, has been suggested as another possibility (Tung, 1931), but no comparable cardiographic changes have been found in other forms of anæmia of a similar degree of severity

Myocardial disturbance In advanced hypothyroidism there may be a reduced cardiac output and enlargement of the heart, which might well modify the shape of the T wave (Means, 1925, Sherf and Boyd, 1945), but similar cardiographic changes have been found in the early stages without

any obvious cardiac failure (Ohler and Abramson, 1934) Myxœdematous swelling of the muscle fibres and connective tissue of the myocardium is the principal post-mortem change discovered, and it is this no doubt that produces the main effect on the cardiogram (Ord, 1880, Schultz, 1921, Ohler and Abramson, 1934, Misske, 1936, LaDue, 1943) [*]

Arteriosclerosis of the heart is quite common in adult myxœdema and could partly account for the cardiac disturbance (Fishberg, 1924, Christian, 1925, and Feldman, 1936) Coronary disease may thus be responsible for persistent alterations in the R–T segment or T wave deflexions occasionally remaining despite treatment (Ohler and Abramson, 1934, and Fournier, 1942)

PRESENT INVESTIGATIONS

The present investigation was carried out to ascertain whether electrocardiography can be of any diagnostic assistance in hypothyroidism in infants and young children, particularly when clinical evidence is doubtful In the course of these studies we were able to place increasing reliance on the abnormal type of tracing discovered, to watch the cardiogram revert to normal under treatment, and ultimately to use it as a control of the optimum amount of thyroid required Our studies were made on 24 cases, 6 boys and 18 girls, in whom either cretinism or myxœdema had been diagnosed, depending on the age of onset Both are encountered in childhood, the one dating from birth but only becoming evident round about the third month, and the other appearing later in a previously healthy child Myxœdema is relatively less common than cretinism, both were found to produce the same cardiographic picture

The cases fall into two groups —10 in whom a cardiogram was taken before thyroid treatment was begun and 14 who were already under treatment before this examination was made

Details of the 10 untreated cases in the first group are summarized in Table I Seven of them were under the age of one year when first examined In their appearance all 10 showed typical signs of hypothyroidism with a protruding tongue, dry skin, thickened subcutaneous tissues, an umbilical hernia, hoarse cry, slow snaky movements, and constipation A delayed bone age was found when radiological examination was carried out

The electrocardiogram was abnormal in all cases the most constant finding being a low voltage curve In addition, changes in the R–T segment were noticed in 8 cases which we came to regard as characteristic These changes appeared either as a

[*] See also Report of the Committee of the Clinical Society of London (1888) and for animal experiments (Goldberg, 1927)

TABLE I

Ten Cretins. Electrocardiograms taken before Treatment was Started

Case No and sex	Date	Present age (years)	Clinical signs	Main electrocardiographic findings	Blood cholesterol (mg %)	Total daily thyroid (grains) showing increasing dosage
1 F	12/9/47	2/12	⊥ +	Low voltage, R–T III abnormal	214	0 2
	31/6/48	11/12	—	Normal		1 0
2 M	14/4/48	2/12	⊥ ⊤	Low voltage R–T I and II abnormal, T I and II negative	216	0 5
3 F	17/8/48	6/12	⊥ ⊥	Low voltage, R–T I and R–T II abnormal		0 75
	7/9/48	7/12	+	Q III deep, otherwise normal	134	0 75
4 F	29/10/46	6/12	+ ⊥	Low voltage R–T II abnormal, T I diphasic	185	0 2
	15/7/47		—	Normal left axis deviation	160	1 5
	7/11/47	20/12	—	Normal, left axis deviation		1 5
5 M	25/3/47	6/12	⊥ ⊥	Low voltage	143	0 25
	1/4/47		⊥ ⊥	Same as 25/3/47		0 4
	3/6/47		⊥	Q III deep, otherwise normal		0 75
	21/7/47		±	Normal		1 5
	10/12/47		±	Normal, left axis deviation	174	1 5
	6/4/48	19/12	±	Normal	176	1 5
6 F	14/4/48	10/12	⊥ +	Low voltage, R–T II and R–T III abnormal	188	0 5
7 F	31/3/47	12/12	⊥ ⊥	Low voltage, paroxysmal ectopic rhythm		0 75
	25/5/47	14/12	⊥	Normal, left axis deviation	146	1 0
8 M	14/6/48	2	+ ⊤	Low voltage, R–T II abnormal	462	0 25
	17/7/48		±	Normal		1·0
9 M	22/7/48	6	⊤ ⊥	Low voltage, R–T I and R–T III abnormal	346	1·0
	30/7/48		+ +	Voltage increased, R–T III abnormal, occasionally S–A block	322	1 0
	10/8/48		+ +	Normal rhythm Same as 30/7/48		0 5
	19/8/48		±	Voltage increased, R–T III abnormal		1 0
	24/8/48		+	Same as 19/8/48	333	0 75
	30/8/48		+	S–T III almost normal	258	1·0
	6/9/48		+	Same as 30/8/48	190	1 5
	21/9/48		±	Same as 30/8/48, left axis deviation	183	2 0
					185	
10 F	18/3/47	8¼	+ +	Low voltage, R–T II and R–T III abnormal	246	1·0
	8/4/47		+ ⊥	Voltage increased normal		1·0
	7/11/47		+	R–T II and R–T III abnormal		1 0
	6/1/48		±	T III negative, otherwise as 7/11/47, low voltage	200	1 5
	3/2/48		±	R–T II and R–T III almost normal		2 0
	13/4/48	9¼	—	Normal	164	2 5

sloping take off of the segment from the descending part of the initial complex or as a convexity of the segment A negative T wave in standard leads I and II was recorded in Case 2 only

Further cardiographic examinations were made during the course of thyroid treatment in 8 cases and the tracings were all found to revert almost or quite to normal in a relatively short time, in Case 3 for instance after 3 weeks treatment Fig 1 to 4 taken from Cases 3 and 8 are typical examples of the cardiographic changes and alteration in appearance of the children before and after treatment

Arrhythmias were observed in two instances ectopic paroxysmal contractions in the first record of Case 7 and sino-auricular block on one occasion during the course of treatment in Case 9

Blood cholesterol was estimated in 8 cases before treatment was begun and was found to be above 200 mg per 100 ml in 5 and below this level in 3 cases

FIG 1 —Appearance of the child (Case 3) before and after treatment with thyroid (0 75 grains a day) for two months

FIG 2.—Appearance of the child (Case 8) before and after treatment with thyroid for three months The dose was gradually increased to 1 grain a day

A	B	A	B	A	B	C
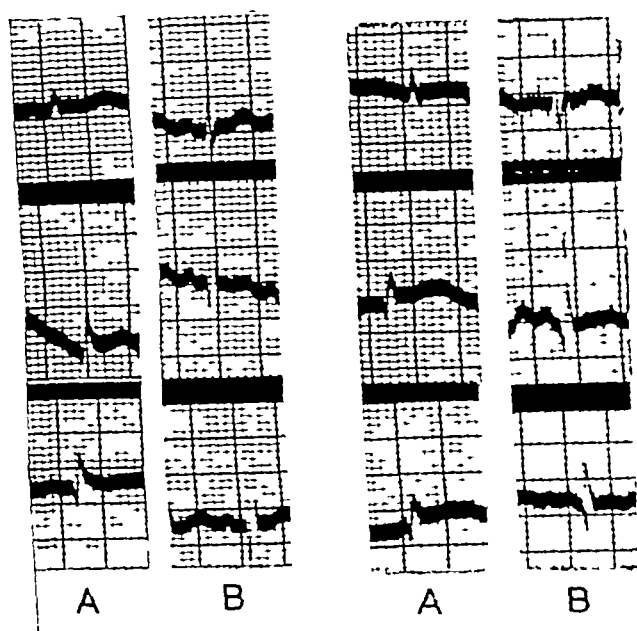
| FIG 3 | FIG 4 | FIG 5 |

FIG 3—Electrocardiograms of Case 3, aged 6 months   Standard leads   (A) 17/8/48   Before treatment   Low voltage curve and alterations in the S–T segments   (B) 7/9/48   Three weeks after treatment with thyroid (0 75 grain a day)   Normal tracing

FIG 4—Electrocardiograms (standard leads) from Case 8, aged 2 years   (A) 14/6/48   Before treatment   Shows the characteristic changes in cretinism   (B) 17/7/48   After treatment with thyroid for one month (dose gradually increased to 1 grain a day)   Normal tracing

FIG 5—Tracings illustrating insufficient thyroid dosage   Standard leads from Case 15, aged 10 years   (A) 19/2/47   Normal electrocardiogram after treatment with thyroid (3 grains a day)   (B) 2/12/47   Changes appearing after decreasing thyroid to 2 5 grains daily for nine months   (C) 20/4/48   Electrocardiogram has again become normal after increase of thyroid to 3 5 grains a day for two months

Data concerning 14 cretins in the second group are summarized in Table II   When first seen they all had the characteristic clinical appearance, but treatment had been started before the first cardiogram was taken and in 13 obvious signs of hypothyroidism had disappeared   The cardiogram was normal in 9 cases and in Case 12 the only change, a right axis deviation, was related to a congenital malformation of the heart which was a complicating factor

INSUFFICIENT DOSAGE OF THYROID

An abnormal curve was recorded at one period of our study in 4 children of this group (Cases 11, 15, 18, and 22) and in each instance this was found to be related to inadequate dosage of thyroid

In Case 11 treatment was begun without delay but in inappropriate amounts, 0 1 grain daily for a month, subsequently reduced to 0 1 grain a week At the age of 7 months when the child first came under our care she still had a cretinous appearance and the cardiogram showed the typical abnormalities already described   The blood cholesterol level, however, was not raised   Thyroid was then increased to 1 5 grains a day and the cardiogram became normal

Case 15 was first seen at the age of 17 months, having been on a dose of 3 grains of thyroid a day for 3 months   A cardiogram taken at that time was normal   During the following years her hospital attendance was irregular and thyroid was reduced to 2 5 grains a day   We next saw her at the age of 10 years, normal in appearance, and we only realized that her thyroid level was sub-optimum when cardiograms in succession began to reveal a low voltage curve and changes in the R–T segments The dose of thyroid was increased to 3 5 grains a day, whereupon the cardiogram again became normal (see Fig 5A–C)

Case 18 had no obvious clinical symptoms beyond

TABLE II

FOURTEEN CRETINS   ELECTROCARDIOGRAMS TAKEN AFTER TREATMENT WAS STARTED

Case No and sex	Present age yrs mths	Thyroid therapy				Electrocardiogram	Blood cholesterol (mg per 100 ml)
		Begun at yrs mths	Further Therapy				
			Date	Daily dose (grains)			
11 F	— 7	— 3	1/6/47	0 4		Low voltage inverted P III	132
			11/9/47	1 5		Low voltage inverted P III	140
			10/5/48	2 0		Normal	
12 F	1 6	— 6	15/4/48	0 5		Right axis deviation, extra systoles	165
			29/7/48	1 0		Normal rhythm	
13 F	1 —	— 4	3/7/48	0 25		Normal	181
14 M	1 —	— 8	20/1/47	1 0		Normal	169
15 F	10 6	1 2	15/3/38	3 0		Normal, left axis deviation	
			19/2/47	2 5		Inverted P III, left axis deviation	
			2/12/47	2 5		Low voltage, R–T II abnormal	
			9/3/48	3 5		Normal left axis deviation	140
			20/4/48	3 5		Normal, left axis deviation	
16 F	2 —	— 8	5/1/48	1 5		Normal	206
17 F	2 —	1 3	8/6/48	1 5		Normal	199
18 F	3 —	— 3	15/6/48	1 0		Low voltage, S–T II and S–T III abnormal	220
			27/7/48	2 0		Normal	161
19 F	4 —	— 4	1/7/47	1·0		Normal	167
20 M	4 2	2 4	2/7/48	1 0		Normal	
21 F	5 3	— 9	3/6/47	2 0		Normal	196
22 F	6 3	2 —	24/5/48	2 0		Low voltage	460
			28/6/48	2 0		Normal	120
23 F	8 4	— 7	16/7/48	1 5		Normal	
24 F	11 2	1 5	15/9/47	1 5		Normal	

Only Cases 11 and 12 still showed a slight appearance of cretinism   Case 12 also had evidence of a congenital malformation of the heart   In Case 22 thyroid treatment had been omitted for one month when first investigated

a slightly increased cholesterol level   Here again electrocardiography betrayed a subthyroid state and after 5 weeks increased dosage abnormalities in the cardiogram and blood cholesterol figure disappeared

A similar sequence of events occurred in Case 22 Thyroid which was taken in adequate doses for four years had been omitted for one month   The cardiogram then taken showed a low voltage curve   The blood cholesterol was among the highest observed (460 mg per 100 ml) and yet there were no marked clinical features   The tracing as well as the cholesterol level became normal one month after resuming thyroid treatment at the same dosage

Case 10 in the first group should also be included as a further example of inadequate therapy regulated by electrocardiographic control (see Fig 6A–D)

Fuller details of these five cases will be found in Tables I and II

A   B   C   D
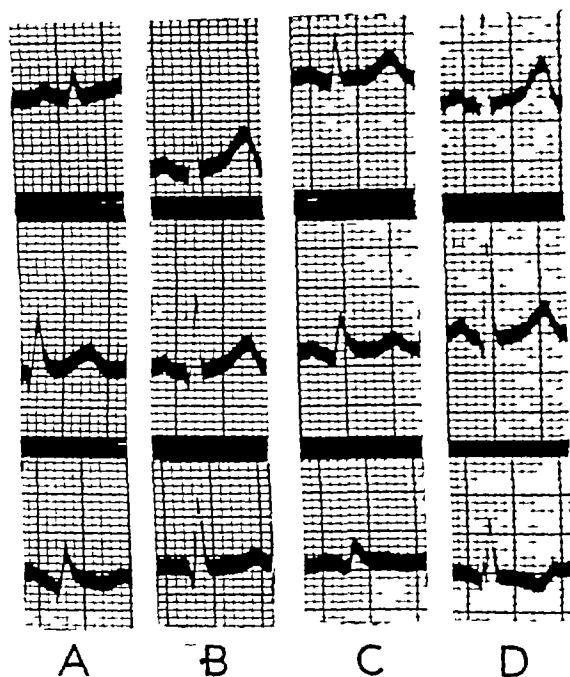
FIG 6 —Tracings illustrating insufficient thyroid dosage
Standard leads from Case 10, aged 8 years
    (A) 18/3/47   Characteristic changes before treatment was started
    (B) 8/4/47   Normal tracing after thyroid, 1 grain a day for three weeks
    (C) 7/11/47   Seven months later   Thyroid dosage still 1 grain a day   The original changes have reappeared
    (D) 13/4/48   The thyroid dosage has gradually been increased to 2 5 grains a day for five months, and the curve is normal again

Electrocardiographic Analysis

The main data are summarized in Table III

Heart rate   The average heart rate of the 10 untreated cretins was 107 a minute the lowest figure being 91 a minute (Case 6) In fact no marked bradycardia was observed but during the course of treatment the heart rate increased somewhat in all these cases The greatest fluctuation occurred in Case 8 where the rate rose from 100 to 140 a minute after one month s thyroid administration In the cretins under treatment the mean heart rate was 121 a minute a figure in the upper limit of normal for this age

Sinus arrhythmia   The degree of sinus arrhythmia was estimated by the method of Schlomka and Reindell (1936) and was found to be diminished in untreated cretins in fact the heart beat in this condition, although slower in rate was found to have the regularity of a 'foetal rhythm

As a rule sinus arrhythmia become more evident during treatment and in the children who had been taking thyroid for some time before they came under observation it was within normal limits

Voltage deflexions   Care was taken to standardize the string tension correctly (1 mv /1 cm) before each tracing was taken and between each lead The mean values of the various elements are shown in Table III and it is obvious that QRS and T deflexions are considerably smaller in untreated cretins than in healthy children A negative T wave in lead III was seen in 8 cases, but by itself we do not regard this as abnormal and Hafkesbring *et al* (1937) found it present in 40 per cent of healthy children

TABLE III
Low Voltage Electrocardiography Deflexions in Twenty-four Cretins

	Standard leads	No of cases	Average age (years)	Heart rate	P mv	Q mv	R mv	S mv	T mv
Group I	Before treatment I				0 04	0 05	0 34	0 13	0 14
	II	10	$2\frac{1}{12}$	107	0 10	0 12	0 58	0 03	0 17
	III				0 05	0 15	0 44	0 01	0 05
	After treatment I				0 11	0 04	1 01	0 23	0 30
	II	8	$3\frac{8}{12}$	132	0 15	0 13	1 10	0 16	0 31
	III				0 04	0 32	0 65	0 16	0 04
Group II	After treatment I				0 10	0 04	0 79	0 31	0 28
	II	14	$2\frac{6}{12}$	121	0 14	0 07	0 82	0 10	0 27
	III				0 06	0 19	0 57	0 10	0 02

Normal figures for comparison
Average height of R (standard leads), normal infants 0 7, 0 9 and 0 7 mv , children of 3 years 1 2, 1 5 and 0 8 mv
Normal height of T I and T II, in infants 0 29 and 0·34 mv , in younger children 0 37 and 0 35 mv
(Nadrai, 1938, and Mannheimer, 1940)
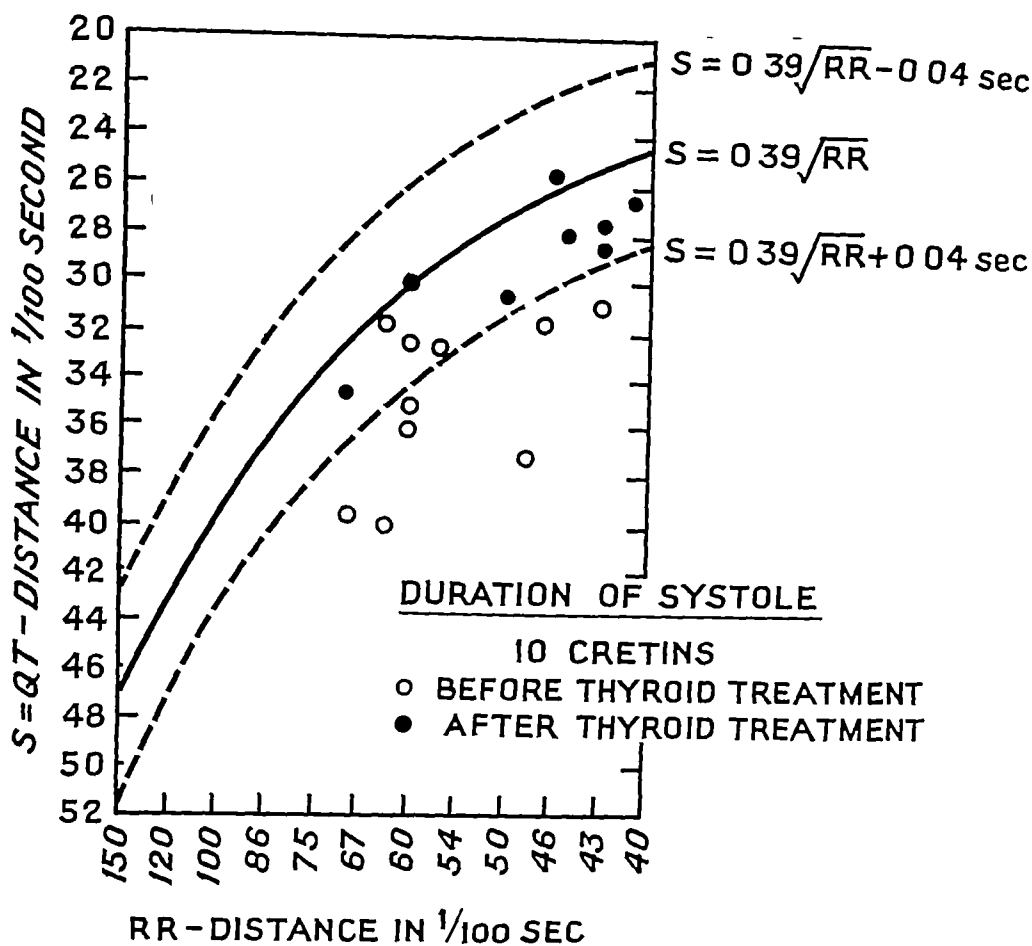
FIG 7 —The duration of systole in 10 cretins before and after thyroid treatment   It was increased in most of the untreated cretins and became normal after thyroid therapy

——— Mean values in normal subjects
– – – – Normal range of variation

During the course of treatment the low voltage curves disappeared and QRS and T resumed their normal shape and height fairly rapidly   This is also true of the P waves, particularly in lead I, although it should be realized that wide variations exist in normal children (Burnett and Taylor, 1936)   The Q waves in lead III also tended to increase when thyroid was administered, but this was not seen in the first two leads

In addition, left axis deviation appeared for a time in 5 cases   In fact it can become permanent and in one girl who has been under our care since infancy on regular and adequate thyroid therapy, left axis deviation is still present at the age of 17 years   although clinically and radiologically the heart appears normal and there is no evidence of left ventricular hypertrophy

P–Q and Q–T intervals   The P–Q interval usually decreased slightly during treatment, the greatest change being from 0 16 to 0 12 sec (Case 9)   The mean values of the P–Q interval did not, however, show any obvious difference in the various groups included in Table III

The duration of systole was calculated according to a formula suggested by Hegglin and Holzmann (1937)   These authors have shown that normal values of the duration of systole (length of Q-T) plotted against the corresponding frequency of ventricular contractions (RR interval) will lie in an area on a graph limited by two lines and expressed
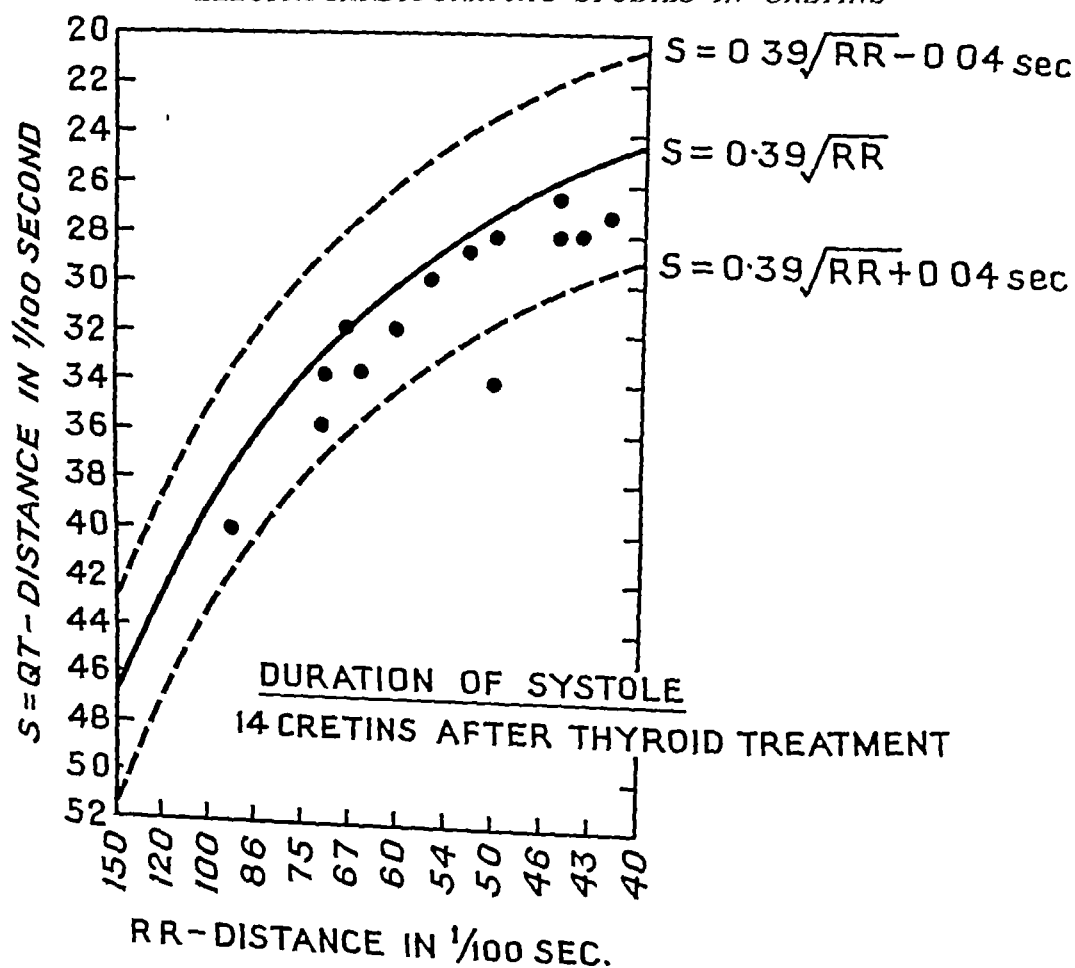
FIG 8 —The duration of systole in 14 cretins after thyroid treatment The figure shows that it was normal in all except one case of those cretins who had been treated with thyroid before the electrocardiogram was taken.

——— Mean values in normal subjects
- - - - Normal range of variation

as a mathematical formula, $0.39 \sqrt{cycle} \pm 0.04$ sec Using this method the length of systole has been plotted on a graph in the case of 10 cretins before and after treatment (Fig 7)

The duration of systole was clearly prolonged in 7 cases before treatment and came within normal limits after thyroid had been given A corresponding calculation was made in the 14 children who had already received treatment before cardiographic records were taken (Fig 8) The duration of systole here was prolonged in only one instance

DOUBTFUL CASES OF CRETINISM

Occasionally cases arise in which an infant's appearance suggests cretinism but the absence of a completely characteristic clinical picture raises

doubt in the diagnosis In such circumstances we have found the cardiograph a great help

Two cases can be quoted An infant was brought to us with a large tongue protruding since birth and an umbilical hernia, but with no other clinical evidence of hypothyroidism A tentative diagnosis of cretinism had been made which was rather shaken when the blood cholesterol was found to be normal (115 mg per 100 ml) and X-ray examination showed a normal bone age A normal cardiogram was the deciding factor, a diagnosis of simple macroglossia was made, no thyroid administered and the child subsequently developed normally with a tongue reduced to the right size

Another child was originally admitted to the hospital for seborrhœic eczema and gastro-enteritis
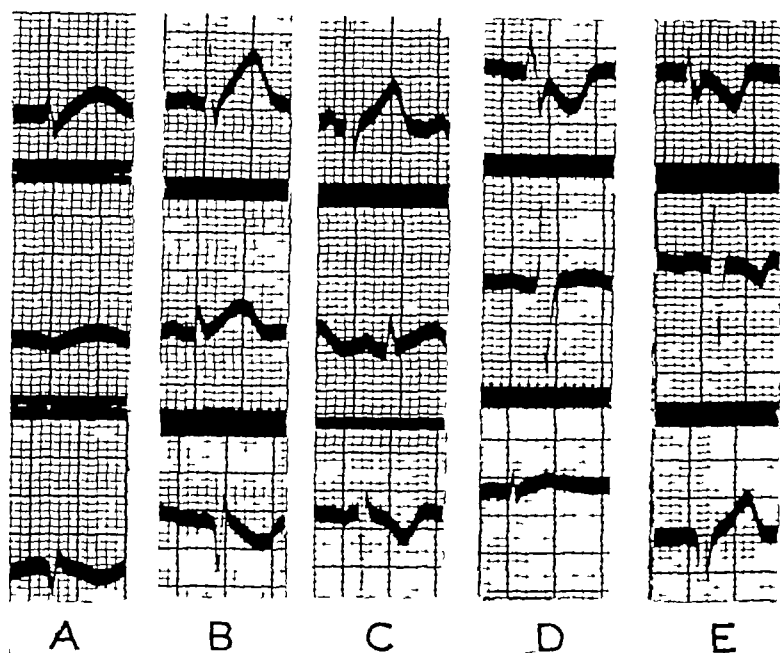
Fɪɢ 9 —Electrocardiograms from Case 9, aged 6 years (A) 22/7/48 Standard leads taken before treatment show the characteristic changes of cretinism (B) 24/8/48 One month after treatment with thyroid (1 grain a day) Voltage increased, abnormalities in R–T segments disappearing. (C) 21/9/48 One month later, dosage of thyroid has been increased to 2 grains a day Left axis deviation, otherwise almost normal tracing (D) 30/7/48 Three unipolar chest leads taken one week after beginning of the treatment with thyroid (1 grain a day) Abnormal S–T segments in V 1, flat upright T in V 2 and low voltage curve in V 5 (E) 21/9/48 Three unipolar chest leads after two months treatment with thyroid (dosage gradually increased to 2 grains a day) S–T segment deviations in V 1 less marked, inverted T wave in V 2 and voltage increased in V 5

The general appearance at that time also suggested a slight degree of hypothyroidism, a diagnosis also favoured by an increased blood cholesterol level Thyroid therapy was given for four months, but when two early cardiograms in succession were found to be quite normal, treatment was stopped with no detrimental effect on the child's subsequent healthy development

DISCUSSION

These studies have shown that characteristic changes in the electrocardiogram occur in untreated cretins which are reversible in a comparatively short time on thyroid administration If the dosage is interrupted or becomes inadequate cardiographic abnormalities reappear Alterations in cutaneous resistance are probably partly responsible for the cardiographic changes because the voltage of the deflexions is considerably increased by the use of subcutaneous leads, a phenomenon we have also observed in normal subjects Such myxœdematous skin infiltration can, however, only play a minor part Changes in the R–T segment, which are also present in unipolar chest leads, and prolongation of systole could not be explained on this basis (see Fig 9A–E)

Pericardial effusion, occurring at times in adult myxœdema, has not been encountered by us in cretins, and arteriosclerosis of the coronary vessels has not had time to develop at this age and cannot therefore be responsible for the R–T changes Anæmia is also not a contributory factor, it is never profound and more than once the cardiogram was observed to return to normal during treatment without any corresponding improvement of the blood count Nervous factors may have some effect on the cardiac action in cretins and the low degree of sinus arrhythmia present may be partly

an indication of this (Landtman, 1947), but from all the evidence direct involvement of the myocardium seems to be the most likely cause of the main cardiographic changes Myxœdematous infiltration causes the heart muscle to swell and is likely to interfere with its action Thyroid treatment rapidly restores the heart to normal and in this way the pathology is somewhat reminiscent of the heart in beriberi which quite rapidly becomes normal when appropriate treatment is given without delay (Weiss and Wilkins, 1937)

and the changes found are described Evidence is brought forward of the value of this method of investigation in regulating the dosage of thyroid required and in the diagnosis of doubtful cases The possible cause of these changes is discussed and evidence is produced pointing to direct myocardial involvement

SUMMARY

Studies of the electrocardiogram were carried out on 24 infants or young children with hypothyroidism

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THE EFFECTS OF THIOCYANATE ON BASAL AND SUPPLEMENTAL BLOOD PRESSURES

BY

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Despite the many conflicting reports published regarding the effect of thiocyanate on high blood pressure it has been shown (Alstad, 1948) that there were indications that in certain patients high blood pressure may be reduced by such treatment Allusion was made to the impression that the fall was due to a reduction in both the basal and the supplemental pressure, taking basal to mean the pressure recorded after the removal of certain stimuli both intrinsic and extrinsic, and supplemental to refer to the part of the casual blood pressure that reflects the physical, emotional, and metabolic activity of the patient at the time (Alam *et al*, 1943)

Thirty-two patients, selected because of a certain degree of hypertension, were investigated and were treated with potassium thiocyanate in doses varying from 0 3 to 0 9 g daily, most of them for over nine months The average age of the group was 56 years, twenty being over 50 years, and eight over 60 years of age Females predominated over males, the ratio being 21 of the former to 11 of the latter No patient was rejected because of complications of hypertension such as encephalopathy, angina pectoris, or previous cardiac failure The casual pressures were recorded in a separate examination room after the patient had been recumbent for a few minutes, basal blood pressures were taken in hospital after a night's rest assured by hypnotics, as described by Kilpatrick (1948) During treatment blood was removed weekly for serum thiocyanate estimation until a desired level was obtained, thereafter the estimations were carried out at longer intervals

The dose of a therapeutic agent varies from patient to patient and in such an investigation as this the drug must be used in an effective amount, hence the difficulty of determining a control series exactly comparable To overcome this it was decided to attempt to control the patients against themselves, achieving this by replacing the drug with a placebo similar in appearance and in taste but containing no thiocyanate This was done only after a significant fall in blood pressure had occurred or after the patient had been treated for at least three months, that is at a time when such a fall might have been expected Care was taken to continue the routine of examination and blood sampling in a manner exactly comparable to that adopted when thiocyanate was being given It was possible to arrange this control in 27 patients, the remaining 5 being omitted because of discontinuance of treatment due to change of location or of some complication of therapy The results are shown in Table I

BASAL BLOOD PRESSURE REDUCTION

The basal blood pressure being recorded under conditions calculated to remove the effect of intrinsic and extrinsic stimuli, *is probably a very reliable measure of the minimum pressure to which the cardiovascular system is subjected* It indicates the level to which the casual pressure may fall and is the guide to the fixity or lability of the hypertension according as the difference between it and the casual pressure is small or great In the 32 *patients examined an interesting relationship exists between the basal and casual pressures as shown in Fig 1* Those patients with high casual pressure tend to have associated high basal pressure, indicating that an increase in the basal pressure is responsible, in part at least, for the high casual pressure in hypertensives

Reduction of the basal blood pressure in any way, if produced by simple methods, would be of considerable importance to hypertensive patients It is known that this may be effected by sympathectomy though not necessarily permanently That a reduction may be produced in some cases by thiocyanate is seen from the fact that in 20 patients or 62 per cent, a fall in basal pressure of greater
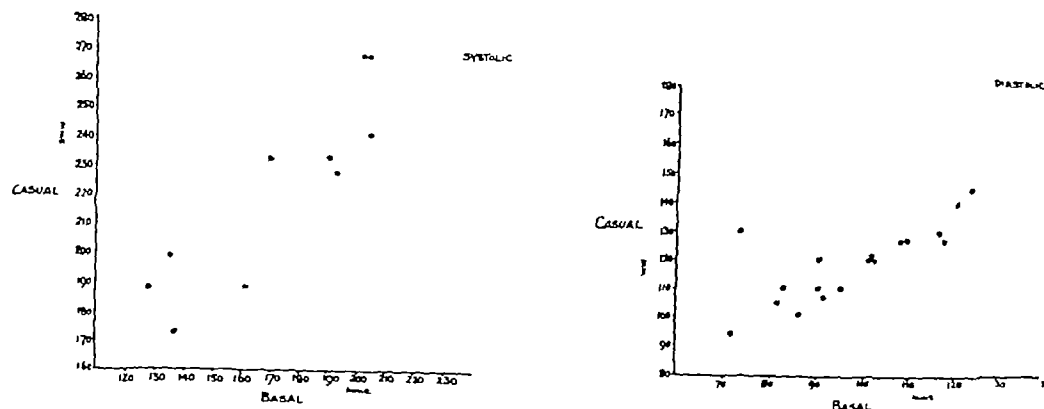
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FIG 1 —Relationship of initial basal pressure to initial casual pressure

TABLE I

REDUCTION OF BLOOD PRESSURE IN THIRTY-TWO PATIENTS TREATED WITH POTASSIUM THIOCYANATE AND WITH A PLACEBO

Case No	Initial pressure			Reduction with treatment			Reduction with placebo		
	Casual (CI)	Basal (BI)	Supplemental (SI)	Casual (CI−CT)	Basal (BI−BT)	Supplemental (SI−ST)	Casual (CI−CP)	Basal (BI−BP)	Supplemental (SI−SP)
1	190/110	128/84	62/26	65/30	40/32	25/0	20/0	+6/0	26/0
2	215/135	170/116	45/19	47/22	30/16	15/11	15/15	12/4	3/11
3	184/104	132/82	52/22	64/24	36/18	28/6	34/4	18/8	16/+4
4	232/128	170/106	62/22	52/20	24/10	28/20	32/16	+4/+10	36/22
5	228/132	170/108	58/24	60/32	38/30	12/2	18/12	12/4	6/8
6	230/120	172/102	58/18	40/20	30/18	10/2	10/10	+4/+4	14/14
7	180/110	142/94	38/16	40/22	20/20	20/2	30/16	6/6	24/10
8	240/124	210/112	30/12	65/24	28/12	30/12	18/4	0/+6	28/10
9	188/108	160/90	28/18	44/20	30/16	14/4	18/0	4/+2	14/2
10	213/130	142/74	71/56	63/40	22/14	41/26	43/40	8/2	35/38
11	210/140	176/122	34/18	40/30	28/10	12/18	10/10	+4/+6	14/16
12	225/163	183/131	42/32	35/33	47/39	0/0	14/19	4/0	8/17
13	254/140	204/120	50/20	44/30	18/18	26/12	22/10	+6/0	28/10
14	235/140	190/120	45/20	45/20	44/18	1/2	5/8	6/0	+1/8
15	230/130	168/120	62/10	70/40	36/30	34/10	36/10	14/0	12/10
16	241/137	163/85	78/52	42/37	41/13	1/24	7/15	5/+5	2/20
17	170/131	137/100	33/31	41/43	15/12	26/31	20/36	+3/6	23/30
18	185/110	141/92	44/18	41/20	25/10	16/0	20/0	1/6	19/+6
19	193/128	153/114	40/14	33/18	17/12	16/6	13/10	+3/+2	16/12
20	185/120	145/102	40/18	35/20	15/12	20/8	15/10	4/2	11/8
21	211/123	163/102	48/21	30/23	11/2	20/22	0/4	2/0	0/1
22	200/95	136/73	64/22	32/20	0/7	36/14	20/4	0/7	25/0
23	200/120	136/90	64/30	40/20	0/0	40/20	30/10	+4/+4	34/14
24	239/125	171/107	68/18	29/22	17/5	12/10	9/12	3/3	8/8
25	275/146	186/114	89/32	35/10	14/12	12/8	9/6	0/0	8/8
26	220/120	192/106	28/14	30/10	18/2	12/14	10/0	2/0	8/2
27	231/130	193/115	38/15	20/10	0/0	23/14	10/10	0/2	13/8
28	242/121	227/125	15/0	21/9	0/3	0/0	—	—	—
29	209/120	185/115	24/5	20/10	8/0	2/6	—	—	—
30	234/117	189/104	45/13	24/16	16/5	18/0	—	—	—
31	263/145	217/127	46/18	30/15	13/23	14/0	—	—	—
32	265/161	199/140	66/21	9/10	14/12	0/0	—	—	—
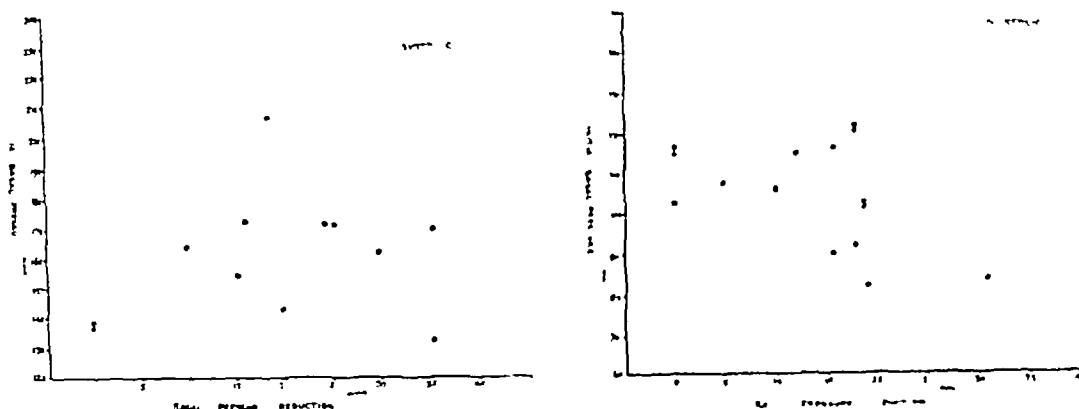
FIG 2 —Relationship of basal pressure reduction to initial basal pressure

than 15/10 mm was produced In 12 of these the reduction was greater than 25/15 mm Falls in basal pressure less than 15/10 mm were disregarded, for although work in this department has shown the basal blood pressure to be a physiological constant in normal individuals and in hypertensives to be much less variable than the casual pressure it was felt that variations less than 15/10 mm might come within the possible range of hypertensive fluctuation The average fall was 25 8/15 7 mm in the 20 cases mentioned while in the remaining 12 the average fall was 10/6 mm If the fall in basal pressure is correlated with the initial basal blood pressure as in Fig 2 there is an indication that the greater reductions tend to occur in patients with lower and moderate basal pressures This tendency might be expected for one would anticipate high basal pressures in those with fixed hypertension and with more advanced pathological changes, and this is what obtained in this series as will be shown in another section

With the use of a placebo the results were uniform no matter the extent of the reduction, the basal recordings with a placebo were similar to those before treatment commenced (cf Fig 3A) That the lowered basal pressure during treatment returned to within a few millimetres of its former level is taken to mean that the drug alone must account for the reduction, else with a placebo the pressure would not have returned consistently to the previous level Had the basal pressure under the influence of a placebo not come back to the initial level (as will be seen occurred with the supplemental pressure) influences other than thiocyanate might have been responsible for the fall There were three instances in which the reduction of basal blood pressure was maintained or returned very slowly to former levels even after thiocyanate was withdrawn

completely for periods of up to three months during which no other treatment was given Apart from the possibility of the initial readings not being truly basal a simple explanation seems to be that the effect of thiocyanate in these cases greatly outlasted its presence in the blood This prolonged effect has been noted by other investigators (Kurtz *et al*, 1941, Fischman 1948) Thiocyanate appears to act by altering some internal mechanism, an action usually operative during its administration only but which is sometimes protracted

SUPPLEMENTAL BLOOD PRESSURE

The supplemental blood pressure may be regarded as an index of the effect of various extrinsic stimuli acting on the patient at the time of recording This part of the casual pressure has been shown by Smirk (1944) to be a variable independent of the basal pressure and accountable in the hypertensive for about one half of the increase above normal of the casual pressure (Smirk, 1944) With the removal of the excitatory causes as in sleep or with the conditions under which the basal pressure is recorded the supplemental pressure will approximate to zero at which level the blood pressure would, of course, be basal That the supplemental pressure of a group of hypertensives would fall with any treatment, medicinal or psychological, might be anticipated as affecting the physical and emotional reactions of the patient In the patients under observation the average supplemental blood pressure was 48/22 mm or about the level already noted in studies on hypertensives conducted in this department (Kilpatrick, 1948) Under treatment the average supplemental pressure was reduced to 27/12 mm The fact that, in all patients who were given a placebo, the supplemental pressure with it
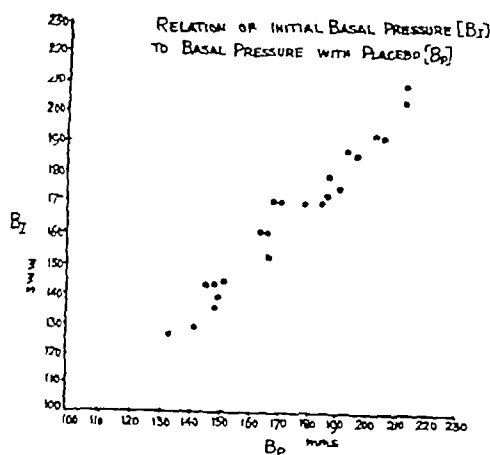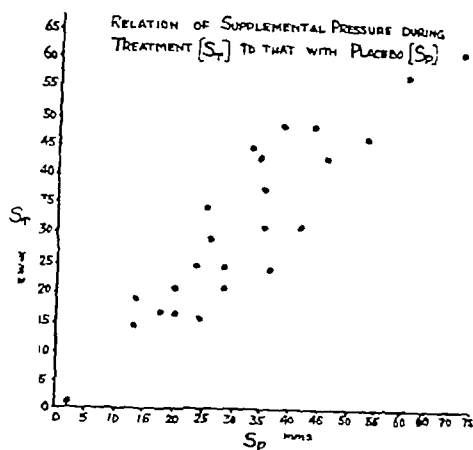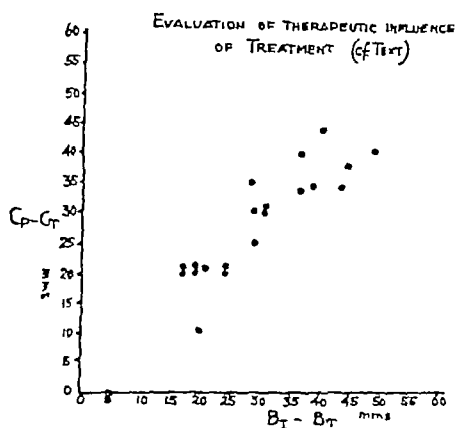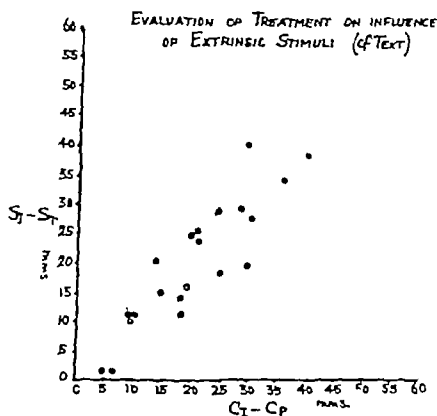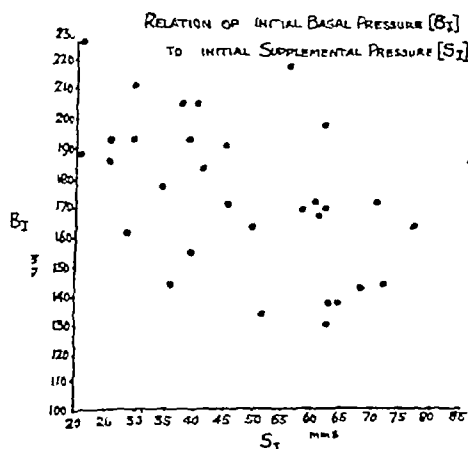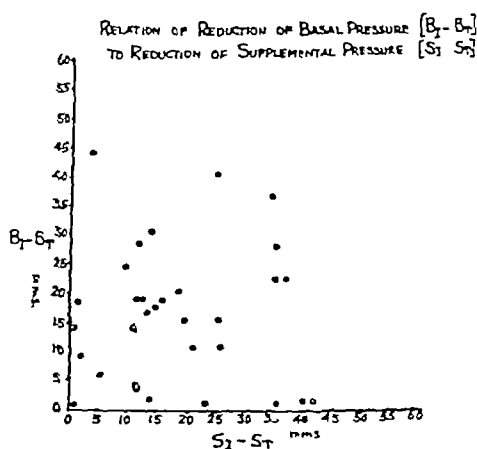
FIG 3 —(A) Relation of initial basal pressure (BI) to basal pressure with placebo (BP)
        (B) Relation of supplemental pressure during treatment (ST) to that with placebo (SP)
        (C) Evaluation of therapeutic influence of treatment (of text)
        (D) Evaluation of treatment on influence of extrinsic stimuli (of text)
        (E) Relation of initial basal pressure (BI) to initial supplemental pressure (SI)
        (F) Relation of reduction of basal pressure (BI–BT) to reduction of supplemental pressure (SI-ST)

approximates to that during treatment (cf Fig 3B) indicates that the reduction affected in supplemental blood pressure is a psychological one, for one could not expect an alteration in the influence of emotional stimuli when the patient is unaware of any change in the regime or medicine If the effect were otherwise the supplemental pressure would be greater with a placebo than with the use of thiocyanate The supplemental pressure fall in those patients with no significant alteration in basal pressure represents the total effect of thiocyanate therapy and therefore is due only to the psychological effect of treatment The psychological effect of thiocyanate therapy therefore may be estimated by the difference between the initial supplemental pressure (SI) and that with a placebo (SP) This measure of the influence of thiocyanate in the supplemental pressure as opposed to its effect on the basal pressure may be shown arithmetically to equal the difference between the initial casual pressure (CI) and the casual pressure with a placebo (CP) since the casual pressure by definition is the sum of the basal and supplemental pressures and as the basal pressure under treatment and with a placebo is the same The relationship in this series between the differences of the initial casual and supplemental pressures and those with a placebo, CI–CP and SI–ST, respectively, is indicated in Fig 3D in those patients whose reduction in pressure was significant, the formula CI–CP allowing of a more direct estimate of the psychological influences of treatment of patients in whom, for any reason basal recordings are unobtainable Again as the supplemental pressure with thiocyanate and with a placebo have been shown to be approximately the same (cf Fig 3B) it follows (because the casual pressure is the sum of the basal and supplemental pressures) that the measurement of the direct effect of thiocyanate (BI–BT) will be the same as the difference between the casual under treatment and with a placebo (CP–CT) so allowing of a measurement of this influence without the necessity of having recordings of the basal blood pressure That this relationship is present in this series is seen by scrutiny of Fig 3C These relationships are present only when there is a significant fall in pressure with treatment

When the relationship of the initial basal and supplemental pressures is regarded (cf Fig 3E), it will be seen that there is a tendency for higher basal pressures to be associated with lower supplemental pressures, e g of 10 basal pressures over 180 mm 8 were associated with supplemental pressures less than 45 mm , while of 18 under 180 only 6 had associated supplemental pressures less than 45 mm A possible explanation may lie in the fact that most

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of the patients whose basal blood pressure was over 180 mm were those in whom pathological changes were more advanced and therefore the cardio vascular system would be less able to reflect the effects of extrinsic stimuli Smirk (1944) found the basal and supplemental pressures were substantially independent variables in a group of patients with essential hypertension selected for the absence of congestive heart failure and other complications Kilpatrick (1948) showed that when heart failure occurred the supplemental pressure was reduced in greater degree relative to the basal It is not surprising, therefore that in the present series of cases including both groups that some of the more advanced hypertensives with heart failure or impending failure have lower supplemental pressures

It would be likely is the effect of thiocyanate on the supplemental pressure is independent of the effect on the basal that the reduction effected in the former would bear no relation to that produced in the latter this is indicated in Fig 3F which shows the basal pressure reduction plotted against the fall in supplemental pressure

It would appear, therefore that the effect of thiocyanate therapy on hypertensives in reducing blood pressure is a direct one as measured by the fall in basal pressure and also an indirect one as measured by the reduction in supplemental pressure the combination of influences being responsible for the alteration produced in the casual blood pressure

At this juncture one may conveniently regard the blood pressure reductions in the light of the extent of pathological change evident in the patients examined All the patients in this series showed evidence of pathological changes associated with hypertension, whatever the aetiology, and this may be because the average age was over 55 years All patients except two had some degree of cardiac enlargement involving the left ventricle which was of the typical hypertensive shape, it was possible to classify the enlargement as minimal, moderate, and considerable Electrocardiography showed left axis shift in all cases, with a varying degree of left ventricular strain in over 50 per cent, particularly in those with large hearts As the retinal vessels are the only ones capable of direct examination it was largely on the basis of retinal vascular change that the following clinical classification of the patients depends Four subdivisions seemed practicable namely

Group 1 (a) Minimal retinal changes in the shape of tortuosity and mild arterial constriction Slight or no cardiac enlargement Left axis deviation

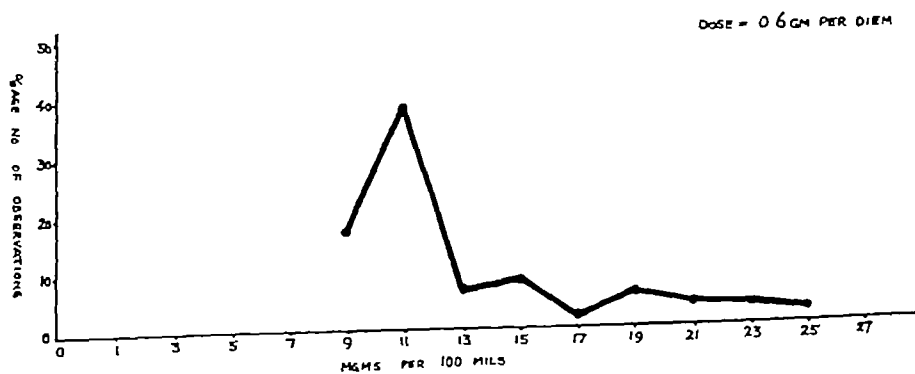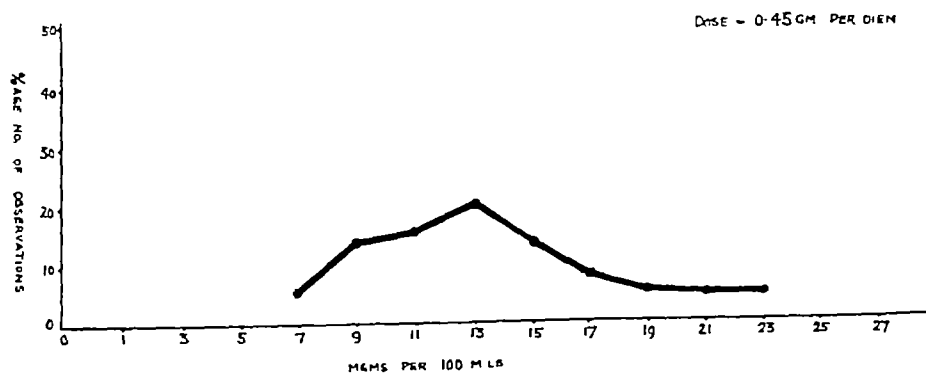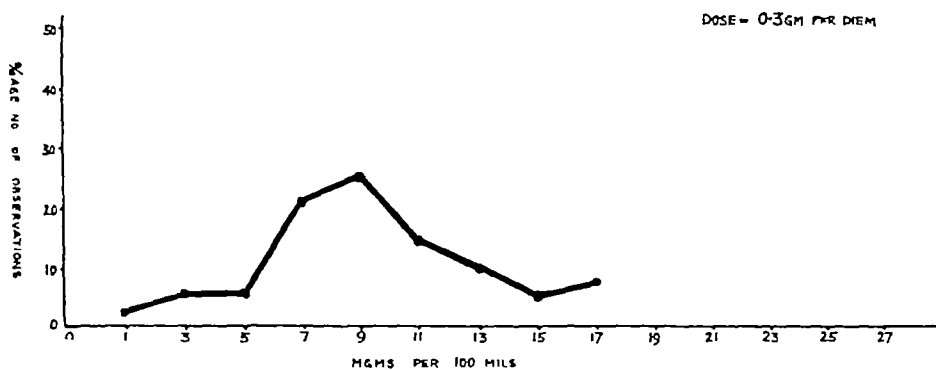*Group* 2 (b) Moderate retinal changes, tortuosity, vascular constriction and nipping of the

FIG 4 —Relationship of thiocyanate serum-concentration to dosage

arteriovenous crossings   Moderate cardiac enlarge-
ment

Group 3   (c) Marked retinal change but without
papillœdema, hæmorrhage or exudate   Cardiac
enlargement usually moderate

Group 4   (d) Marked retinal changes including
hæmorrhage exudate, and papillœdema   Cardiac
enlargement usually considerable

TABLE II

RELATION OF REDUCTION IN CASUAL AND IN BASAL
BLOOD PRESSURE TO ASSOCIATED VASCULAR CHANGE
IN PATIENTS WITH HYPERTENSION

Clinical sub-division (see text)	Number of patients	No showing reduction of Casual pressure of more than 40/20 mm	No showing reduction in Basal pressure greater than	
			20/10 mm	15/10 mm
Group 1	9	7	6	8
Group 2	3	2	1	2
Group 3	15	8	6	9
Group 4	5	1	1	1
Total	32	18	14	20

It will be seen from Table II that *reductions in
casual blood pressure occurred in each group*, but
the incidence of reduction was greater in groups 1
and 2 than in 2 and 3   Indeed, out of 12 patients
in the first two groups 9 had significant falls of
casual pressure while in the latter two groups, 9 out
of 20 patients showed any significant reduction in
pressure   When the basal pressure reductions are
viewed in the light of the degree of pathological
change evident in the patients a similar distribution
is seen   Thus it would appear that reductions in
blood pressure tend to occur more easily in patients
in whom the pathological changes associated with
hypertension are least in evidence, such a conclusion
is in keeping with the findings of Watkinson and
Evans (1947) in this respect

DOSAGE AND BLOOD LEVELS OF KCNS

The dosage of the drug was a variable conditioned
mainly in these patients by the response in blood
pressure reduction   Experience had already shown
that to start at a high dosage was to invite the onset
of complications particularly in the form of rashes
and gastro-intestinal upset, hence the initial dose
was the moderate one of 0 3 g daily   Blood levels
were recorded at weekly intervals using Bowler's
modification of Barker's technique (1944)   If the

blood pressure response were inadequate after four
weeks the dose was increased by 0 15 g daily   It
was found that 0 45 g was the dose usually neces-
sary to produce a reasonable fall in basal and in
casual pressure   If however such a fall did not
occur the dose was again increased in several
instances to 0 9 g daily   Generally the blood level
followed the dose and larger doses were productive
of higher serum concentrations (cf Fig 4)   It was
noted that the lack of response in patients in whom
no satisfactory fall of blood pressure was attained
could usually be attributed to the development of
some complication of thiocyanate e g rash or
diarrhœa early in treatment in which case the drug
was discontinued   Some patients did not have an
appreciable fall in blood pressure despite large doses
of drug and the attainment of high blood concen-
trations, e g over 20 mg per 100 ml   Further-
more in almost all patients in whom the pressure
fall was adequate a dose of 0 45 g daily was sufficient
and this generally produced blood levels in the
region of 8–12 mg per 100 ml (cf Fig 4)   It would
seem therefore that an adequate blood level must
be maintained in the region of 10 mg per 100 ml ,
which is best produced slowly and that if the
patient does not show a fall in blood pressure when
the level is raised to this extent they are most un-
likely to do so by attempting to raise it still higher
In several instances blood levels of over 25 mg per
100 ml were maintained for several weeks without
producing a further fall in blood pressure

Here one would remark that if a careful check is
maintained on the serum level of thiocyanate and
if the patient is seen frequently there appears to be
little danger of untoward effects of therapy   Com-
plications in this series were infrequent and took
the form of rashes and gastro-intestinal upsets in
four cases   In one only were mental symptoms
encountered   As the average age in this series was
55 years it would indicate that age is no contra-
indication to therapy

SUMMARY AND CONCLUSIONS

Selected patients with hypertension have been
treated with thiocyanate over periods varying from
one to twenty months   A reduction in basal blood
pressure of more than 15/10 mm was noted in
twenty or 62 per cent of the patients   The greater
reductions tended to occur with the lower or
moderate blood pressures   This reduction in basal
pressure has been shown to account for a propor-
tion of the casual pressure fall and it has been
suggested that the diminution in basal pressure
represents the effective fall directly due to the
therapy utilized, in this case, thiocyanate

Indications have been given that the effect of the psychological influence of thiocyanate treatment may be measured by taking the difference in casual blood pressure initially and that occurring with a placebo, or by subtracting the supplemental pressure under treatment from the initial supplemental pressure This latter measure of the psychological influence of treatment depending on the conception that the supplemental pressure is an index of the effect of physical, metabolic, and emotional stimuli of which, under the conditions of this investigation, the emotion was the principal factor In addition, the therapeutic effects of thiocyanate might be gauged either by taking the difference between the basal pressure before and during treatment or by the difference between the casual pressure under treatment and with a placebo This was shown to be expressed conveniently by the equation $CI-CP = BI-BT$ where CI and CP respectively were casual pressure initially and with a placebo, and BI and BT were the initial basal and the basal pressure under treatment

It has been shown that greater reductions are to be anticipated in patients in whom permanent pathological changes secondary to the hypertension are not advanced The more these changes are in evidence as judged by heart size, electrocardiogram, and fundal examination, the less likelihood is there of any influence occurring with thiocyanate

The following conclusions can therefore be drawn from this study

The influence of potassium thiocyanate in reducing significantly the casual blood pressure in selected patients with hypertension is due to a diminution in both basal and supplemental pressure

The reduction in basal blood pressure probably represents the direct effect of thiocyanate on the cardiovascular system

The reduction in supplemental blood pressure with thiocyanate is a measure of the influence of this treatment in diminishing the effect of extrinsic stimuli on the patient, and is produced in a manner similar to the effect of a placebo

The larger reductions in basal blood pressure are found in patients in whom pathological changes in the cardiovascular system are not advanced

The optimal serum concentration of potassium thiocyanate is 8–12 mg per 100 ml which may be attained usually by a dose of 0 3–0 45 g daily Toxic effects are commoner with levels above this limit, but with care the serum concentration may be raised to much higher levels without complications, although it is not considered advisable to produce blood serum levels above 12 mg per 100 ml

If the desired effect of thiocyanate therapy is not produced by serum concentrations of 8–12 mg per 100 ml it is unlikely to occur by increasing the dose and the blood level

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RADIOKYMOGRAPHY IN PATENT DUCTUS ARTERIOSUS

BY

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The introduction of radiokymography dates from the pioneer work of Gött and Rosenthal (1912) The modern multiple slit kymograph was developed subsequently by Stumpf and his co-workers (1934), while later studies were made by Faber and Kjaergaard (1936) and Bordet and Fischgold (1937) In an earlier paper one of us (Wood, 1939) described the kymographic patterns that comprise the borders of the normal cardiac silhouette

In the present study, X-ray kymography has been applied to the diagnosis of patent ductus arteriosus The development during the past decade of the surgical treatment of the condition has greatly increased the importance of a diagnosis that may be difficult In some cases the characteristic continuous murmur is not present and according to statistics quoted by Brown (1939) the pathognomonic murmur is absent in more than half of the cases On the other hand Taussig (1947) claims that the diagnosis is based on the finding of a continuous murmur over the pulmonary area and that unless such a murmur is present the diagnosis cannot be made with certainty It is when a murmur confined to systole is heard at the pulmonary area that diagnostic difficulties are likely to arise Differentiation from pulmonary stenosis may not be easy and the possibility that patency of the ductus may be associated with other anomalies has to be remembered It is an essential part of the diagnosis to exclude associated defects since when these exist ligature of a ductus may abolish an important compensatory mechanism As exploratory operations are obviously undesirable, no effort must be spared to determine the correct diagnosis We consider that the radiokymographic appearances which we now present should help to place the diagnosis of patent ductus arteriosus on a secure basis

METHOD OF INVESTIGATION AND RADIOGRAPHIC TECHNIQUE

We have made radiokymographs in every patient in whom a diagnosis of patent ductus arteriosus was made or entertained The majority of these later came to operation and in every instance the diagnosis was confirmed The kymographs were all taken with the moving grid technique at a focus film distance of four feet The grid used has a spacing of 11 5 mm between the horizontal slits At first, an exposure time of 3 seconds was used but later the rate of fall of the grid was increased to give an exposure of 1 8 seconds At this speed satisfactory tracings were obtained with a heart beating at the normal rate, and also in patients with tachycardia

Kymographs in the postero anterior position were taken and these were supplemented by films in the oblique positions especially the left oblique, whenever this appeared desirable A standard exposure time was maintained so that the tracings made were comparable This applied particularly where kymographs before and after operation were contrasted The exposure factors were 65 KVP for children and as much as 90 KVP for full size adults, using 100 milliamperes with a rotating anode tube In sixteen patients operation for ligature of the patent ductus was subsequently undertaken

X-RAY APPEARANCES

The abnormality most commonly found in postero-anterior films of patients with patent ductus arteriosus is a prominence of the pulmonary arc and, in less degree, of the pulmonary conus The cardiac outline may in other instances be entirely normal in patients proved at operation to have the same congenital defect Taussig (1947) has referred to the slight prominence of the pulmonary conus in some normal children, and has insisted that the

diagnosis of patent ductus arteriosus should never be based solely on the contour of the heart   Consequently, the diagnosis must depend largely upon the murmurs unless other means are available, such as radiokymography

The kymographic appearances of the left border of the cardiac silhouette in the normal heart may be summarized as follows   In the ventricular area waves of a certain type are seen, these consist of a curved upper limb due to the slow relaxation of the ventricle in diastole and a more horizontal lower limb representing the rapid contraction in systole Above this is the zone of mixed or confused movements described originally by Stumpf (1934)   This lies between the pulmonary artery waves above and those of the left ventricle below   The aorta and pulmonary artery show characteristic waves which have an almost horizontal upper limb due to lateral displacement by the pulse wave and a sloping lower limb representing the subsequent slower elastic recoil

Light is thrown on the origin of the mixed movements by the kymograph shown in Fig 1 which is taken from a man aged, 70, with complete heart block   There is one large ventricular wave recorded in the left ventricular area in each segment whereas at the lower part of the right border during the corresponding interval of time three distinct waves are seen which can only be ascribed to auricular contractions   In the segment immediately above

the left ventricular region a further three waves can be seen of a similar rhythm which must also be auricular in origin and be ascribed to the left auricle or left auricular appendix which curves forward in this area at the root of the great vessels   This provides evidence that the left auricle may form part of the left border of the cardiac silhouette   It also shows that the mixed movements described must be partly auricular in origin, the other components being the super-imposed pulmonary artery waves This zone of mixed movements must not be confused with the fine vibration waves described below, which lie in the ductus area between the aortic and the pulmonary artery levels

KYMOGRAPHIC SIGNS IN PATENT DUCTUS ARTERIOSUS

In our kymographic study of sixteen patients with patent ductus arteriosus proved at operation, we have observed four special features of the left border of the cardiac silhouette   They are as follows

(1) Para-aortic waves
(2) Vibration waves
(3) Exaggerated pulmonary artery waves
(4) Exaggerated upper left ventricular waves

Of these four signs the first two relate to the lesion itself while the last two are consequences of the hæmodynamic disorder caused by the defect   The features of each sign are described as follows
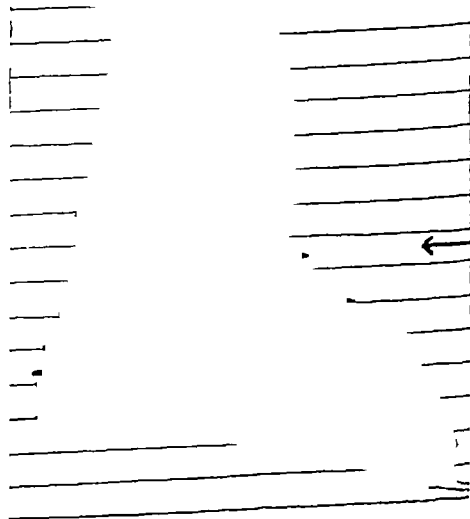
A   B

FIG 1 —Man, aged 70   Complete A-V block   (A) Kymograph   (B) Tracing showing auricular waves
(marked by arrow) on left border of heart

Para aortic waves These are wave forms which lie parallel to and lateral to the aortic knuckle They are less dense than the shadow of the aorta but are usually well seen when present as in Fig 2 These waves differ from the zig-zag vascular shadows often seen well away from the mediastinum in the lung fields, which show transmitted pulsation from the aorta or left ventricle This sign was present in six of our cases It has been encountered in no other condition and we have never seen it in any kymograph taken after ligature of the ductus

Vibration waves These occupy a narrow region immediately below the aortic waves and blend farther down with the pulmonary artery waves They are shown in Fig 3 in which (A) shows the whole kymograph and (B) a magnification of the encircled zone in (A) The fine fibration waves of a frequency of approximately 400 a minute are seen at the centre of the magnified zone Careful scrutiny is often required to detect these waves, by the naked eye in the kymograph The reproduction in Fig 4 shows ill defined vibration waves, but the accompanying drawing made from the film by tracing the outline of the waves from the film, placed over a horizontal viewing box, illustrates them and their

position Fig 5 shows a kymograph taken in the left anterior oblique position The vibration waves are seen in the magnified section on the border of the ascending part of the arch of the aorta a position that is surprising in view of the comparative remoteness from the ductus region However it is difficult to assign any other interpretation to these waves which have been encountered on several occasions in left oblique films

It is suggested that vibration waves constitute a visual radiological counterpart of the palpable clinical thrill and that they are caused by the vibration of the ductus and the adjacent parts of the aorta and pulmonary artery In some of our earlier kymographs, the zone of fine wave forms was not well seen This was due in part to the inherent difficulties of radiography in young children With increased experience of the method and the subject better results were obtained and we have found the zone of fine wave forms to be a frequent feature of the kymograph in patent ductus arteriosus being present in 12 of our 16 cases Moreover in kymographs taken after operative cure of the condition these special wave forms are no longer seen

Exaggerated pulmonary artery waves These are

A
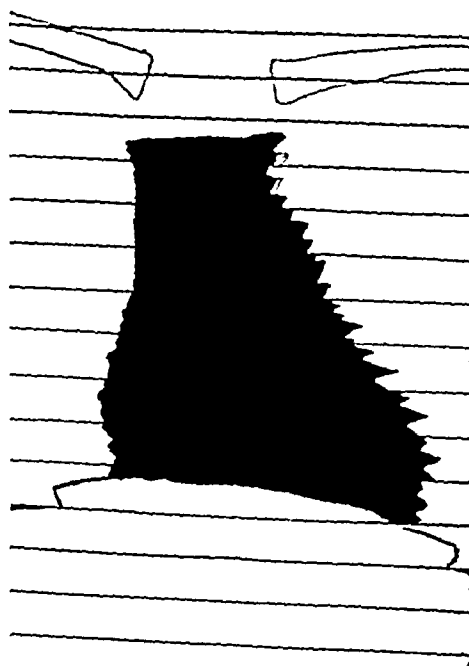
B

FIG 2.—Boy, aged 6 Patent ductus arteriosus (A) Kymograph showing para-aortic waves of the kymograph para-aortic waves shaded (B) Tracing

A

B
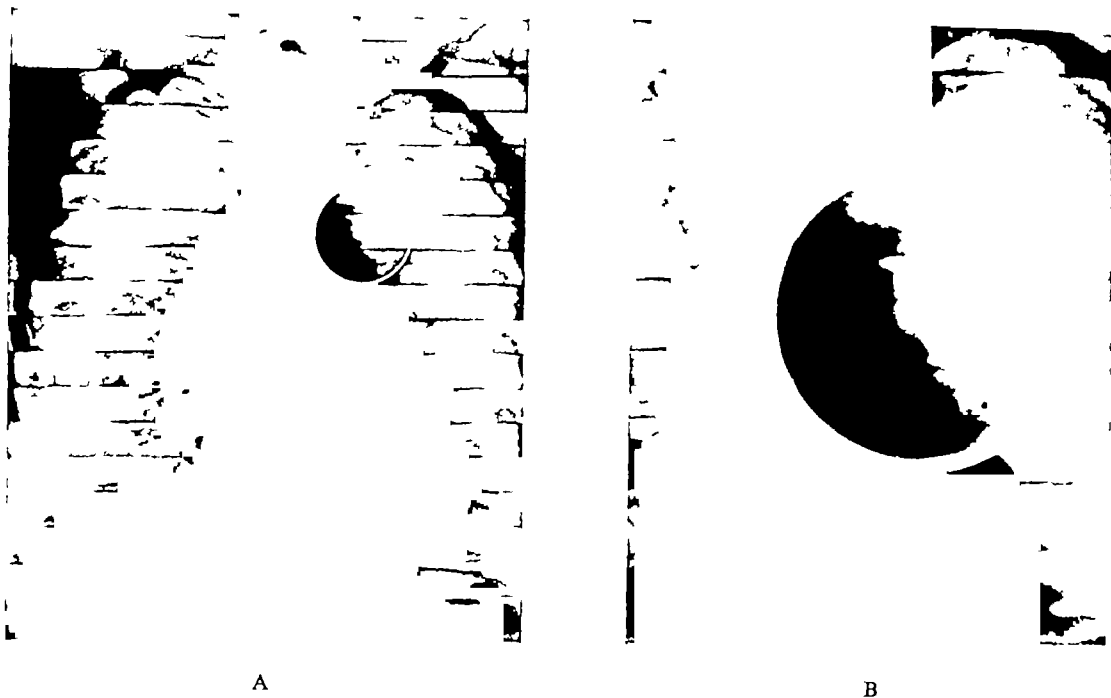
FIG 3 —Girl, aged 6   Patent ductus arteriosus   (A) Kymograph   (B) Magnification of encircled zone in (A) to show vibration waves

A

B
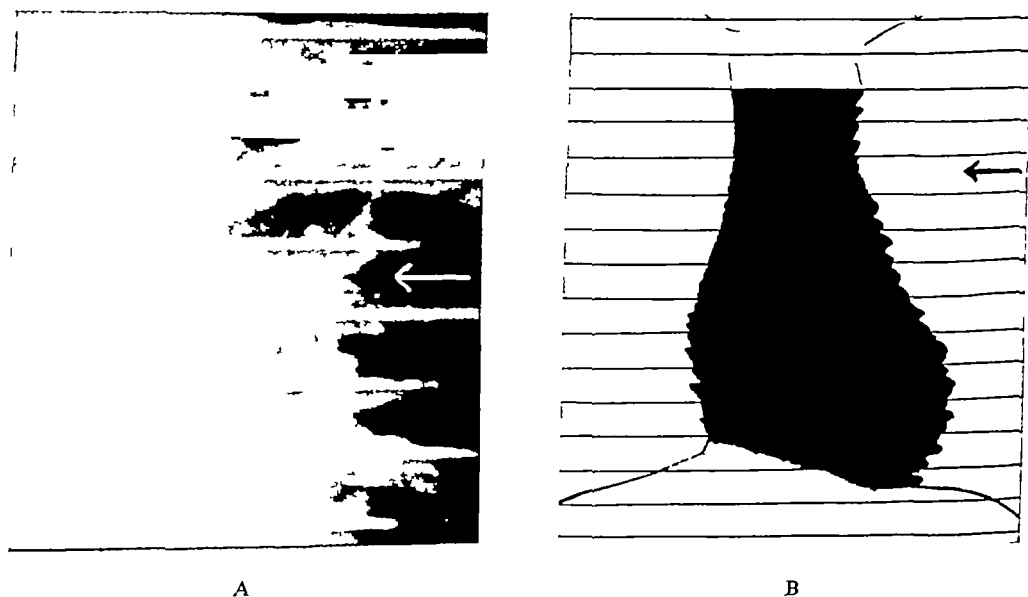
FIG 4 —Boy, aged 13   Patent ductus arteriosus   (A) Portion of kymograph showing ill-defined vibration waves   (B) Tracing of the whole kymograph to illustrate position (arrow)
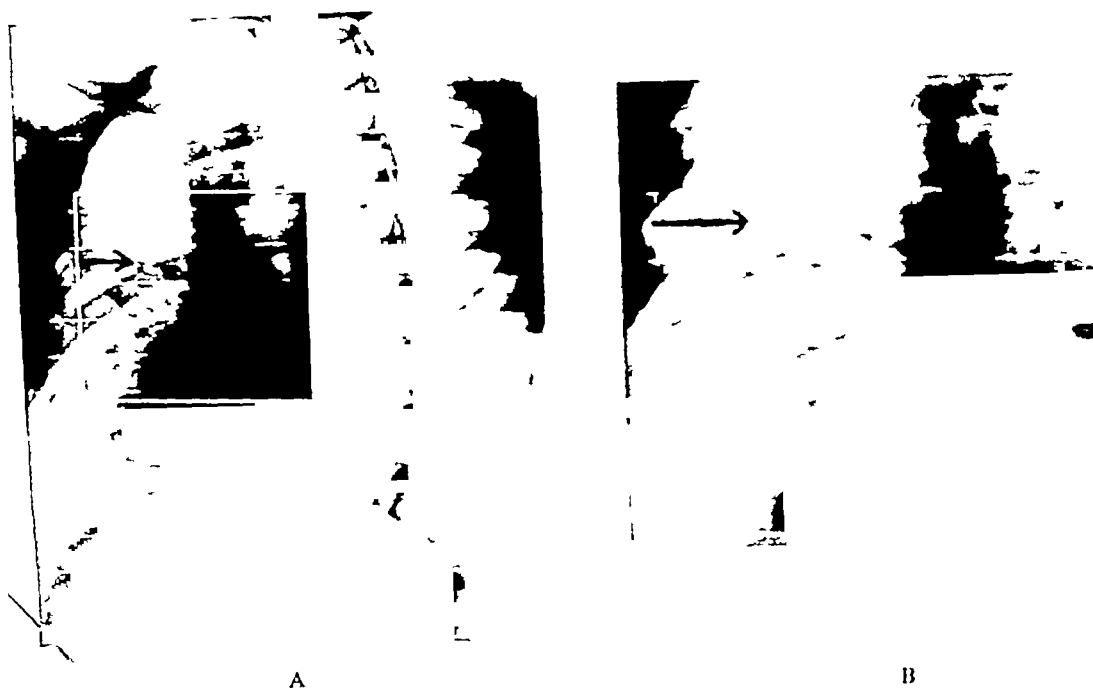
FIG 5 —Girl, aged 7   Patent ductus arteriosus   (A) Kymograph in left anterior oblique position   (B) Oblong marked area magnified to show vibration waves on border of shadow of ascending part of arch of aorta (arrow)
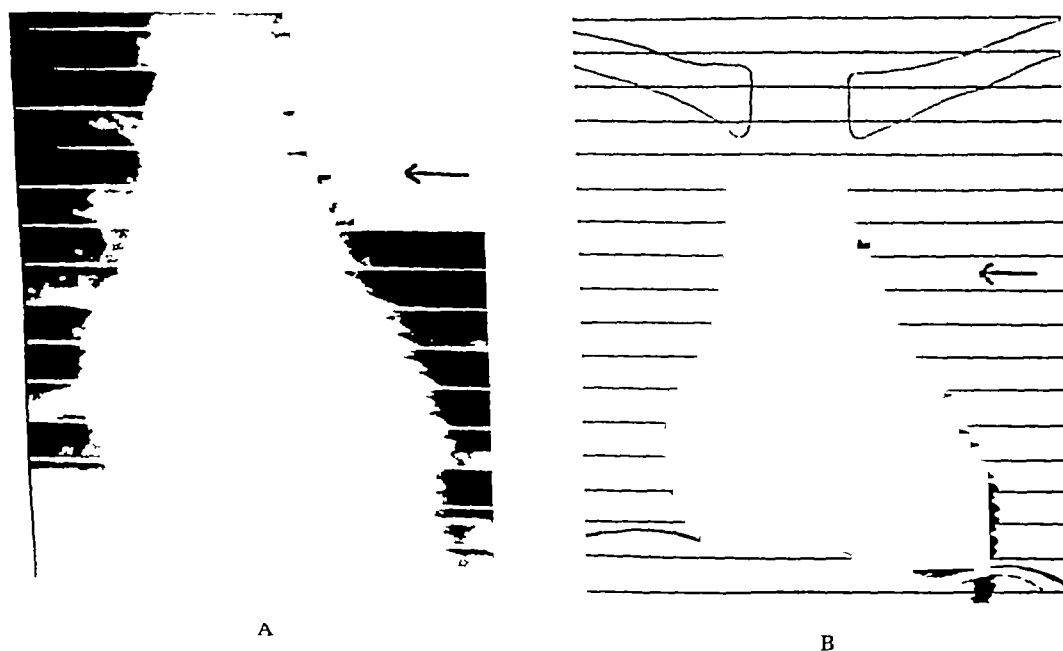
FIG 6 —Woman, aged 30   Patent ductus arteriosus   (A) Kymograph showing slightly convex pulmonary arc with exaggerated waves   (B) Tracing of kymograph to illustrate

A   B
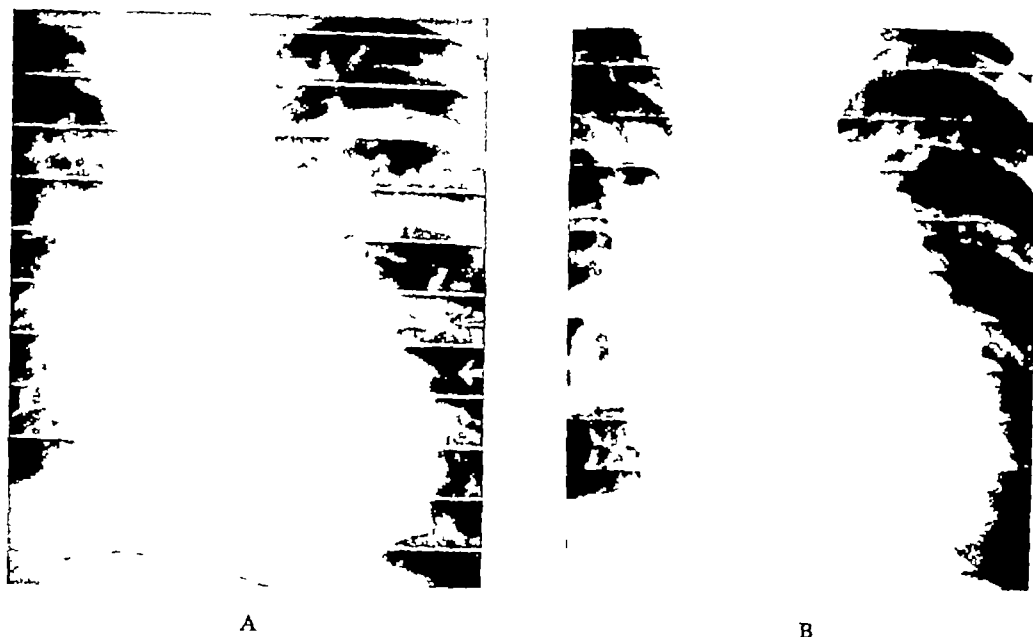
Fig 7—Boy, aged 7   Patent ductus arteriosus   (A) Kymograph showing exaggerated upper left ventricular
     waves   (B) Kymograph of same patient after operation showing disappearance of the abnormally
     large waves

shown in Fig 6A in which the pulmonary arc is slightly convex   The accompanying drawing (Fig 6B) illustrates the essential features of the kymograph   These appearances are in accordance with the prominent and pulsatile pulmonary arc frequently seen on radioscopy   The main branches of the pulmonary artery may also show exaggerated movement corresponding to the hilar dance so often seen on screen examination, this is of value in excluding pulmonary stenosis

Exaggerated upper left ventricular waves   Fig 7A shows very conspicuous wave forms due to the vigorous contraction of the upper part of the left ventricle   Such exaggeration is also seen in aortic incompetence   This is not surprising since both conditions involve a leak from the aorta and may therefore be expected to produce similar hæmodynamic disorders   After closure of the communication between the aorta and the pulmonary artery by ligation of the ductus, these abnormal ventricular contractions disappear, as is shown in *Fig 7B, a kymograph taken after operation*

SUMMARY

Radiokymography has been applied to the diagnosis of patent ductus arteriosus   The series here presented comprises sixteen patients proved at

operation to have this congenital defect   The following four kymographic signs are described

(1) Para-aortic waves lying parallel to and lateral to the aortic zone
(2) Vibration waves situated immediately below the aortic zone and between this and the pulmonary zone
(3) Exaggerated pulmonary artery waves
(4) Exaggerated upper left ventricular waves

The production of these signs is discussed and reasons are given for relating the para aortic and vibration waves to the ductus and the vibration in it and in adjacent structures   On the other hand, the amplification of the waves normally seen in relation to the pulmonary artery and the upper part of the left ventricle is due to the associated hæmodynamic disorder

Reference is made to some of the difficulties in clinical diagnosis   It is considered that radiokymography is valuable in helping to establish conclusively the diagnosis before operation

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MASS MINIATURE RADIOGRAPHY IN THE DETECTION OF HEART DISEASE

BY

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From the Mass Radiography Unit, Glasgow

The Glasgow Mass Radiography Unit began operations in the summer of 1944   Like other such *units in the country, its primary intention was the* early detection of tuberculous lung disease although it was realized that non-tuberculous conditions and *notably heart disease would come within its sphere* The Mass Radiography Sub-Committee of the Minister of Health's Standing Advisory Committee on Tuberculosis, in 1943, laid down standards of cardiovascular abnormalities based on the appearances in full-size chest X-ray films taken after the miniature film had shown an unusual cardiovascular shadow   The abnormal appearances sought were general increase in size of the cardiovascular shadow, increased density of the shadow, displacement of the right cardiac border to the right and of the left border to the left in varying degree, and undue prominence of the large blood vessels

It was soon observed that the postero-anterior large films gave little information that could not be given by the miniature film   The experienced eye could detect enlargement of the cardiac shadow in the *miniature film, making allowance for the greater* distortion at a distance of 36 inches from the X-ray tube focus as against 60 inches   Varying shades of increased density of the cardiovascular shadow itself such as may be caused by the enlarged left auricle of mitral stenosis could also be noted   Accordingly, it became the rule to offer *full clinical examination* to any person found to have an abnormality of the cardiac shadow on the miniature X-ray film

During the initial period of our investigation some *other observations were made   It was often seen,* for example, that prominence of the pulmonary artery shadow did not indicate clinical heart disease It was *therefore, decided to ask certain questions* designed to bring out a history of previous rheumatic infection or of other illness significant in the ætiology of heart disease, and *to discover the numbers of*

people passing through the unit who understood they had some form of heart disease   It was thought that if the X-ray appearances and history could be correlated the findings might be decisive in limiting needless recalls   Also, a history of known heart disease was frequently contradicted by the absence of cardiac abnormality on radiological or clinical examination

After consideration of the experience of the unit in its first year of operation it was decided that the following groups should be recalled for full clinical examination   (1) patients with a history of rheumatic fever, chorea, or other illness *suggestive* of acute rheumatism, (2) those with a history of heart disease, and (3) those with abnormality of the cardiovascular shadow in the miniature X-ray film   It was hoped in this way to ensure the detection of cardiac abnormalities in patients unaware of an existing heart lesion with the minimum of inconvenience   This survey was begun in September 1945, and continued till March 1947, when the direct association of the authors in the work of the unit ceased   An account of the findings follows and certain conclusions are drawn, these should enable the unit, while pursuing its primary purpose of detecting tuberculosis in the community, to have a clearer understanding of the significance of the many cardiovascular abnormalities encountered in the day to day work of the unit

AGE DISTRIBUTION

Fully two thirds of those examined were under twenty years of age and rather more than half under fifteen   The reasons for this distribution are the heavy concentration of the unit on the examination of school-leavers, and the choice for survey of industries in which there is a high proportion of young workers because the highest returns of active pulmonary tuberculosis can be expected in these

groups As regards heart lesions, the expectation from such a distribution is that congenital disease and lesions due to acute rheumatism will predominate but not lesions the result of degeneration hypertension or chronic lung disease The average recall rate for our purpose was about 49 per thousand, it was rather more in females and rather less in males mainly because of the larger recall rate in the well represented group of girls under fifteen

GROUPS RECALLED FOR FURTHER STUDY

Table I shows the relative parts played by history of heart disease, abnormality of the cardiovascular shadow in the X-ray film, and rheumatic history in the recalling of examinees for clinical examination It brings out that a finding of X-ray abnormality was the commonest single cause for recall while a history of rheumatic illness and a history of heart disease were much less common causes

TABLE I

INCIDENCE OF ABNORMAL X RAY HEART SHADOW AND A HISTORY OF HEART DISEASE OR RHEUMATIC FEVER

Total surveyed (both sexes)	34,918
Recalled for heart investigation	1,703
History of heart disease	31%
Finding of X ray abnormality	66%
History of rheumatic illness	44%
History of heart disease + finding of X ray abnormality	11%
History of heart disease + history of rheumatic illness	19%
Finding of X ray abnormality + rheumatic illness	19%
History of heart disease + finding of X ray abnormality + history of rheumatic illness	7%

The percentage figures refer to the number recalled

It was also found that when a history of heart disease was not elicited, a finding of X-ray abnormality was a much more common cause for recall than a history of rheumatic illness The reverse was the case in the group in which a history of heart disease was obtained

THE VALUE OF A HISTORY OF RHEUMATIC ILLNESS

Questions were put by trained clerical staff at the time of the miniature film examination to elicit a history of one or more attacks of rheumatic fever, one or more attacks of chorea or of other illness consistent with acute rheumatism A preliminary investigation had suggested that histories of sore throat blood-poisoning and scarlet fever were too common to be of value although if any one of these was accompanied by arthritis or muscular pains some importance might be attached to it Such rheumatic symptoms are represented in this series under the heading of other rheumatic manifestations All histories were closely checked by the medical examiner at the time of the clinical examination and almost invariably found to be correct

Table II shows the relative frequency of the various types and grades of rheumatic illness in this group A single attack of rheumatic fever was the most frequent finding other rheumatic manifestations were less common chorea was relatively rare There was no great difference between the sexes except that chorea was more common among the females

TABLE II

THE INCIDENCE OF THE VARIOUS GRADES OF RHEUMATIC INFECTION IN THE GROUP RECALLED ON THIS ACCOUNT

	Male	Female	Both sexes
History of rheumatic fever once	219	177	396
History of rheumatic fever twice or more	36	35	71
History of chorea once	17	37	54
History of chorea twice or more	1	7	8
History of rheumatic fever and chorea	13	7	20
History of other rheumatic manifestations	57	143	200
Totals	343	406	749

Table III shows the relationship in the whole series between a history of rheumatic infection and the clinical findings It brings out the greater frequency with which acquired heart disease is associated with multiple attacks of rheumatic fever or chorea and the relative unimportance in respect of organic disease of the group of " other rheumatic manifestations " Equally noticeable is the frequency of normal findings when there is a history of a single attack of rheumatic fever

In patients giving a history of rheumatic infection but not giving a history of heart disease there are few instances of acquired heart disease (21 out of 423 examined) suggesting that in most cases when acute rheumatism causes heart disease that fact is known to the patient On the other hand, in patients giving a history of rheumatic infection and a history of heart disease the opposite obtains, namely, a high incidence of organic heart disease, and this is

	Normal	Non-significant findings	Organic disease
History of rheumatic fever once	234 (54%)	80 (52%)	76 (52%)
History of rheumatic fever twice or more	23 (5%)	12 (8%)	32 (22%)
History of chorea once	30 (7%)	11 (7%)	12 (8%)
History of chorea twice or more	4 (1%)	1 (1%)	3 (2%)
History of chorea and rheumatic fever	9 (2%)	3 (2%)	8 (5%)
History of other rheumatic illness	130 (30%)	46 (30%)	16 (11%)
Total	430	153	147

again most marked where there is a history of multiple rheumatic infection Six cases of congenital heart disease and thirteen of hypertension were also discovered

The group of non-significant findings such as innocent mitral systolic murmurs, or a split first sound at the apex would be expected to run parallel with the group of normal findings if it had no relation to rheumatic illness, if it had such a relationship it should reflect the results in the group of organic disease findings Table III suggests that it has closer affinities with the normal group than with the group of heart disease

THE X-RAY APPEARANCES

The shadows on the 35 mm film, being photographs of the appearances on a fluorescent screen placed at a distance of 36 inches from the focus of the X-ray tube, are somewhat distorted Those placed to the periphery of the photograph are larger than those more centrally placed in comparison with the actual structures within the chest, and also in respect of the fact that tissues within the chest which are close to the X-ray focus, and therefore far from the fluorescent screen, cast larger images than those farther from the X-ray focus Thus in ordinary postero-anterior films in which the patient faces the fluorescent screen with his back to the X-ray tube the shadow cast by the spine or a posteriorly placed tumour will be relatively broader than that of the aorta and that in turn relatively larger than the shadow of the heart or an anteriorly placed tumour Further, cardiac enlargement will

be emphasized and actual enlargement of the heart will never be quite so much as the shadow on the 35 mm film would suggest Another point is that prominences posterior to the heart will be emphasized at the expense of the shadows cast by the lateral borders of the heart so that the pear-shaped increase of density in the heart shadow cast by the hypertrophied left auricle in mitral stenosis will be more obvious than in a film taken at a greater distance than 36 inches

Slight scoliosis may simulate cardiac enlargement in a miniature film and so may slight rotation of the patient Films showing evidence of such deformity or of rotation were not included in this series Table IV shows the frequency with which various radiological abnormalities were found

	Male	Female	Both sexes
General cardiac enlargement	320	299	619
Prominence of pulmonary artery	182	277	459
Straightening of left heart border	41	74	115
Unfolding of aorta	42	45	87
Broadening of base of heart	18	50	68
Prominent conus	65	28	93
Dextrocardia	3	2	5

Table V shows the relationship between radiological general cardiac enlargement, irrespective of degree, and the clinical findings It shows that in only a twelfth of the cases of cardiac enlargement without history of heart disease is there evidence of heart disease, and even where there is a history of heart disease the presence of a heart lesion in such cases is confirmed only in rather more than half the cases (about two thirds of females less than half of males)

The relationship between prominence of the pulmonary artery shadow in the miniature X-ray film and the clinical findings is shown in Table V The pulmonary artery was judged to be prominent if it overlapped a line joining the aortic bulb and the left heart border at ventricular level The Table shows that few cases with prominence of the pulmonary artery have an actual cardiac lesion even in the group with a history of heart disease less than half have been confirmed as in fact having heart disease The same conclusion can be drawn when the clinical findings are related to straightening of the left heart border in the X-ray film

TABLE V

Relationship of X Ray and Clinical Findings

	Normal	Non significant	Organic	Congenital	Hypertensive	Total
Radiological Cardiac Enlargement						
No history of heart disease	297 (72%)	83 (20%)	24 (6%)	4 (1%)	5 (1%)	413
History of heart disease	29 (28%)	14 (14%)	55 (53%)	3 (3%)	2 (2%)	103
Prominence of the Pulmonary Artery Shadow						
No history of heart disease	305 (73%)	96 (23%)	14 (3%)	3 (1%)	—	418
History of heart disease	10 (24%)	13 (32%)	16 (39%)	2 (5%)	—	41
Prominence of Conus						
No history of heart disease	24 (52%)	15 (33%)	6 (13%)	1 (2%)	—	46
History of heart disease	1 (4%)	3 (14%)	18 (82%)	0	—	22

When broadening of the base of the heart shadow (i e the distance between the right border of the superior vena cava and ascending aorta on the right and the descending part of the aortic arch on the left) is related to the clinical findings, it is found that if it is present in association with heart disease the fact of the latter is known to the patient No case of organic heart disease was found in this group in the absence of a history of heart disease The same conclusion could be drawn when clinical findings were correlated with unfolding of the aorta including prominence of the aortic bulb, as might be expected, hypertension was a more common finding in this group

Table V also shows the relationship between prominence of the pulmonary conus and the clinical findings When there is clinical evidence of disease and a prominent conus is noted in the X-ray film,

the patient is usually already aware that he has heart disease At the same time, the frequency of discovery of unsuspected organic disease was higher than with prominence of the pulmonary artery

THE CLINICAL EXAMINATION

The examination of 529 people who believed they had heart disease, revealed no evidence of this in 340 (64 per cent) Table VI shows this and also the incidence of cardiac lesions at different age groups In almost all the cases the examination was entirely clinical, the findings in the erect position, in the supine position, on the left side, and after exertion being correlated The blood pressure was taken if it was considered relevant Only in exceptional cases were further aids to diagnosis, such as radiography in the oblique

TABLE VI

Age Distribution of Examinees and Incidence of Cardiac Lesions in those with a History of Heart Disease

	Age in Years								
	Up to 14	15–19	20–24	25–29	30–39	40–49	50–59	60 and over	Total
Total number (A) (to nearest hundred)	189	46	30	20	28	22	11	3	349
Number with history of heart disease (B)	247	61	35	28	69	38	41	10	529
Percentage of (B) with heart disease	33	34	51	43	38	34	37	20	36

positions or following a barium swallow, electro-cardiography or sphygmography, employed as it was the intention to interfere as little as possible with the routine of the school child or worker Patients were on occasions admitted to hospital for diagnostic purposes or with a view to treatment

The main clinical findings have been sufficiently considered in the preceding sections of this paper It remains to discuss first the group of what has been labelled non-significant findings, and secondly, to give the details of our findings in the "organic disease" group Under the heading of non-significant findings are such final clinical diagnoses as split mitral first sounds, innocent mitral systolic murmurs, split pulmonary second sounds and pulmonary systolic murmurs

The total incidence of innocent mitral systolic murmurs, pulmonary systolic murmurs and split mitral first sounds, is shown in Table VII Of the 1703 cases 798 were males, and 905 females

Split mitral first sound This is probably most commonly confused with the presystolic murmur of mitral stenosis A split first sound was diagnosed in this series when no diastolic element was brought out by change in posture or by exercise, the sound was usually made more evident by exercise and was best heard at the end of expiration when the breath was held As long as its possibility is kept in mind the very different character of the first part of the sound is not likely to be mistaken for a short presystolic murmur In our series it was not commonly associated with X-ray abnormalities Its incidence was 10 per cent in the absence of X-ray abnormality, and 7 per cent in association with such abnormality

It was no more common in patients giving a history of rheumatic fever than in those without such a history, the incidence was 8 per cent in both groups These figures merit the belief that rheumatic infection played no part in the production of the findings We are satisfied that the finding is not a significant one and that its incidence in such a series as this is as high as 8 per cent

Innocent mitral systolic murmurs The certain diagnosis of this group of murmurs is always difficult Where a murmur did not have the properties possessed by the ' organic murmurs," of loudness, propagation, and encroachment on the first sound, it was considered in the light of Evans' classification of innocent murmurs (Evans, 1947) and its relation to the patient's posture, and its position in the cardiac cycle, was studied Phonocardiography was not used

The incidence of the finding was between 5 and 6 per cent in both sexes Its frequency was 5 per cent in the absence of a history of rheumatic infection and 6 per cent when there was such a history —figures so close as to show that rheumatic fever played no part in its causation Among the group who had no reason to believe they had heart disease the innocent mitral murmur was found in rather less than 4 per cent whereas it was found in more than 9 per cent of those who believed they had heart disease The innocent murmur was found in only 4 per cent of those with and in 8 per cent of those without, radiological abnormality Stress should be laid, therefore, on the comparatively common incidence of this murmur, its frequent confusion with the organic murmur," and the absence of

TABLE VII

SHOWS THE INCIDENCE OF MITRAL SYSTOLIC MURMURS, PULMONARY SYSTOLIC MURMURS AND SPLIT MITRAL FIRST SOUNDS IN THE PRESENT SERIES

History of rheumatic infection	None				Rheumatic fever				Other rheumatic manifestations			
History of known heart disease	No		Yes		No		Yes		No		Yes	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present
X-ray abnormality	22	729	130	73	200	85	178	86	17	121	33	29
Total mitral systolic	4	24	13	7	9	3	19	7	0	5	3	1
Total pulmonary systolic	3	76	7	8	13	5	16	4	1	18	2	2
Total split mitral first sound	3	52	14	7	18	3	20	5	1	12	1	1

correlation with a history of rheumatic fever or X ray abnormality

Split pulmonary second sound This finding is not uncommon in mitral stenosis A split pul monary second sound was found frequently in the series of 1703 cases examined and no significance could be attached to the finding at the time of examination These cases are being followed up The exact numbers in the series cannot be given because the great frequency of the finding was not fully appreciated at the start of the investigation and it was not particularly noted at first Latterly the prevalence of this sign in the absence of any discoverable clinical abnormality became obvious and more recent observations have only served to confirm our opinion that it is particularly common and apparently without clinical significance It was about twice as common in males and the incidence was comparable whether there was or was not an X ray abnormality It was almost twice as common when there was a rheumatic history and fully twice as common in those who understood they had heart disease

Pulmonary systolic murmur The murmur was found alone, or in combination with other non-significant findings, in 155 cases (9 per cent) No account is taken here of those cases in which it was heard in association with mitral stenosis It was more common in females—almost 13 per cent as against 5 per cent in males Rheumatic infection was not concerned in its production—8 per cent as against 10 per cent in the absence of such a history While it was found in a considerable proportion of cases understood to have heart disease fully 7 per cent in a total of 529 yet it was found more commonly among those who had no reason to believe that they had a cardiac abnormality (10 per cent of 1174 examined) It was more common in the presence of radiological abnormality than in its absence, the abnormality reported in almost every case was enlargement of the pulmonary artery, resulting in straightening of the left heart border or actual prominence of the artery beyond that line Further, it was most common in the younger age-groups, e g of the 155 cases 110 were under 15 years It was comparatively rare in adult life The probable explanation of the presence of the murmur is that the artery is dilated beyond a normal pul monary ring, and its more common occurrence in the younger age-groups may be associated with the greater distensibility of the soft and resilient artery in adolescence Increase in the blood flow in the pulmonary artery as brought about by exercise accentuates a murmur already there and often brings out a murmur not heard previously The importance and significance of this murmur must

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be recognized Prominence of the pulmonary artery is much more commonly associated with it than with organic mitral disease

ORGANIC DISEASE

Of the 1703 cases examined 220 (just over 12 per cent) were found to have organic heart disease (Table VI) The bulk of these had mitral valve disease a few had aortic valve disease, and the remainder were found to have auricular fibrillation coronary occlusion or myocarditis Mitral valve disease was found in 185 (11 per cent) and aortic valve disease in 13 (less than one per cent), three patients had both aortic and mitral valve disease

The incidence of normal findings among those believed to have heart disease has been stressed but it should be noted that a diagnosis of organic valve disease was occasionally made for the first time in the course of the routine work of the mass radio graphy unit Mitral valve disease was diagnosed in 41 cases and aortic valve disease in 3 Of the 41 with mitral disease 21 gave a history of previous rheumatic infection Therefore only 20, all of whom had abnormal X-ray findings would have been found in the series relying solely on the lead given by the radiological picture One only of the three patients with aortic disease was discovered because of X-ray abnormalities (in the other two there was a history of rheumatic infection) Twenty-one cases therefore of organic valve disease were discovered as the result of abnormal radiological appearances in 34 918 routine X-rays of the chest

SUMMARY AND CONCLUSIONS

In the course of the routine working of the Mass Radiography Unit in Glasgow many abnormal cardiovascular shadows were encountered Of these the most common were general cardiac enlargement, prominence of the pulmonary artery straightening of the left heart border, unfolding of the aorta, broadening of the base of the heart, prominence of the pulmonary conus and dextrocardia In an effort to limit needless recalls an attempt was made to correlate the various radiological abnormalities with a history of previous rheumatic infection or known heart disease

Of 34,918 cases X-rayed by the unit in the course of the investigation, fully 67 per cent were under 20 years of age Altogether 798 males (4 3 per cent) and 905 females (5 5 per cent) were recalled Of the 1703 recalled the commonest cause of recall was an unusual X-ray picture, a history of previous rheumatic infection was a less common cause of recall, and least common was a history of known heart disease All three reasons for recall were present in 115 cases (almost 7 per cent)

A history of one attack of rheumatic fever was associated with a finding of organic heart disease in, roughly, only one in five cases   two or more attacks resulted in clinical evidence of disease in rather less than half the cases giving such a history   This is a low incidence, but it must be realized that no strict check could be made on the accuracy of the history of rheumatic fever,   many comparatively minor febrile illnesses masquerade under this heading   Although the numbers were smaller, it was found that one attack of chorea resulted in organic heart disease slightly more often than did one attack of rheumatic fever   Patients with a history of previous rheumatic infection and found to have heart disease mostly knew of it, apart from examples of hypertension   only 23 cases were found to have heart disease not previously known to them—21 with organic valve disease, 2 with congenital heart disease

Radiological cardiac enlargement was associated with organic heart disease in 93 cases (out of 516 in whom this X-ray finding was reported)   Prominence of the pulmonary artery shadow was not a common cause of heart disease being brought to light for the first time,   only 14 cases of acquired and 3 of congenital disease were found in this way out of 418 examined   Prominence of the conus, though less frequently diagnosed in the film, was more likely to be supported by clinical evidence of organic disease, than was a prominent pulmonary artery

An outstanding finding was that no evidence of disease was found in 340 out of 529 patients who believed they had heart disease (64 per cent)

The frequency of non-significant findings such as split mitral first sounds, mitral systolic murmurs, split pulmonary second sounds, and pulmonary systolic murmurs is noted and their relationship with radiological abnormalities and a history of rheumatic infection described

Of the 1703 cases examined 220 were found to have acquired organic heart disease,   of these 185 had mitral disease, 13 aortic disease, and 3 both mitral and aortic disease   Only 41 cases of mitral disease and 3 cases of aortic disease were found in which the disability had been unknown to the patient   Of these, 20 with mitral disease and one with aortic disease were referred solely on account of the radiological findings   Thus only 21 cases of organic valve disease were diagnosed for the first time in 34 918 routine X-rays of the chest

In conclusion the common radiological patterns sometimes thought to be suggestive of heart disease are not, as a rule, associated with clinical signs of disease   Such patterns by themselves do not suffice for a diagnosis of heart disease

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THE ELECTROCARDIOGRAM OF POSTERIOR
CARDIAC INFARCTION

BY

PETER MEYER

In suspected coronary artery disease, no clinical sign can as yet displace the electrocardiograph which, by revealing past cardiac infarction, provides objective evidence for the diagnosis, much reliance must, therefore, be placed on the electrocardiographic signs of infarction   In lesions of the anterior wall, the signs are often characteristic, especially in chest leads   Posterior infarction is shown by deep and wide Q deflections by significant R–T deviation, and by T inversion in lead II and III, and in the unipolar left leg lead   In the absence of coronary R–T changes the signs of posterior infarction may be uncertain since inversion of T in lead III, and occasionally also in lead II, may occur without infarction, and Q in lead II and III and in the unipolar left leg lead may be equivocal   The practical experience of diagnostic difficulties has led to the present study which is to show the close similarity of certain types of cardiograms representing posterior infarction to tracings taken from patients without infarction, and to examine records of infarction for additional electrocardiographic signs that might be helpful in the interpretation of equivocal curves

The object of the analysis was the form of the QRS complex, in which changes due to infarction could be expected to last longer, and to be more specifically characteristic of this lesion, than changes in the T wave   In the absence of necropsy control, care was taken to include cardiograms only if the clinical diagnosis was firmly established   Patients with cardiac infarction gave a typical history of pain, and showed the classical changes of posterior infarction in the standard leads   With one exception (Fig 3F), cardiograms were rejected if the signs of infarction were confined to the R–T segment and the T wave and did not include a small Q in lead III, if the cardiogram was equivocal, the diagnosis was accepted only if it was confirmed by serial tracings   Infarction was held to be absent if there was no history of pain and if the age and clinical condition

provided no suspicion of coronary disease   in a number of cases the clinical diagnosis was further supported by the presence of changes in serial cardiograms   Most of the tracings reviewed were taken in private practice with a Siemens electrocardiograph which registers time in 0 05 second some of the patients were seen at the National Heart Hospital under the care of Dr William Evans   The records of 40 patients with posterior infarction were analysed

I   ELECTROCARDIOGRAMS WITH EQUIVOCAL CHANGES OF THE QRS COMPLEX IN THE STANDARD LEADS

Of 40 patients with posterior infarction 7 had standard limb leads with Q deflections in lead III, or II and III, which did not differ in size or depth or both from similar Q waves seen in patients without infarction   The cardiographic signs that caused uncertainty in the interpretation of the curves varied with the position of the long axis of the heart   In concordant cardiograms, showing mainly upright QRS complexes in the standard leads as seen when the heart was in the ' vertical   position according to Wilson's terminology, Q II and Q III were of uncertain significance if they were less than 0 04 second in width and if the amplitude of Q III was less than 25 per cent of the tallest R in any limb lead   Cardiograms with a similar QRS pattern were seen in patients without infarction   In the tracings illustrated in Fig 1 the infarct could not be recognized by the appearance of the Q waves or by any other change in the QRS complex, the presence or absence of S waves in lead I had no relation to the diagnosis, but Q I was more likely to be present when there was no infarction

In discordant cardiograms, with QRS mainly upright in lead I and downward in lead III, Q was equivocal if it was deep, or deep and wide, in lead III, but small or absent in lead II   Care had to be taken to exclude a false Q III   when each successive beat in lead III was examined, a small R was often
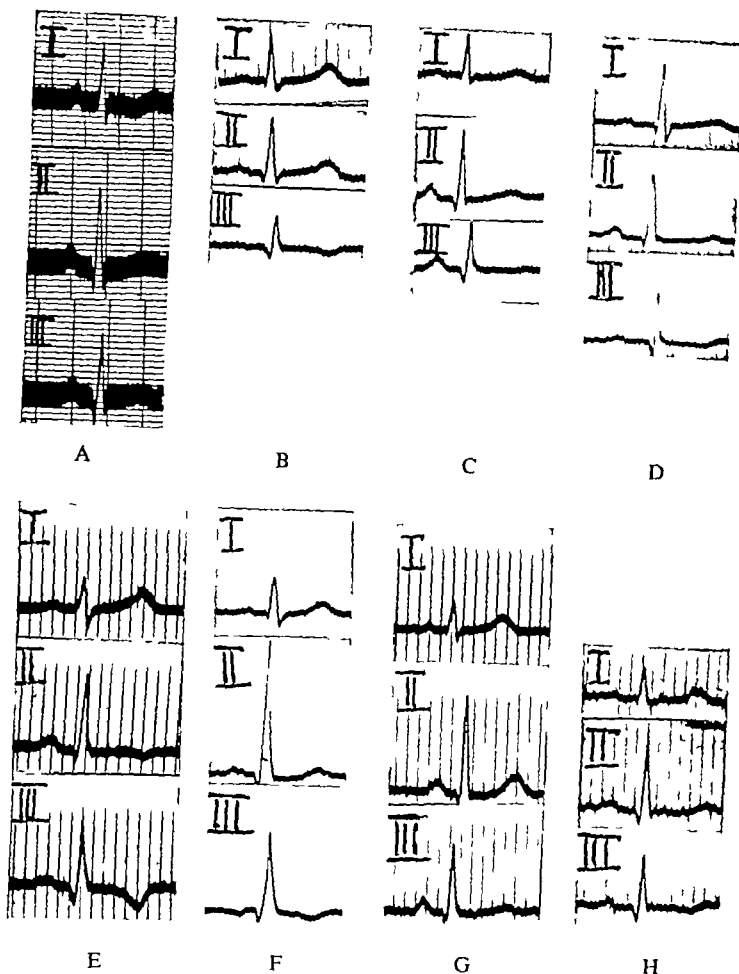
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FIG 1 —Electrocardiograms of the concordant type with equivocal Q deflections

(A) Case 1   Man aged 45   posterior infarction
    (see also Fig 4C)
(B) Case 2   Man aged 36   palpitation
(C) Case 3   Man aged 77   broncho pneumonia
(D) Case 4   Man aged 47   palpitation

(E) Case 5   Man aged 47   posterior infarction
(F) Case 6   Man aged 31   left mammary pain
(G) Case 7   Woman aged 21   extrasystoles
(H) Case 8   Woman aged 57   thyroid toxaemia

found to precede the downward deflection which, in many tracings, was then revealed as an S wave The absolute size of Q III and its size relative to the R waves in other leads, was the same in patients with and without infarction, a wide Q III was more frequent in infarction (Fig 2A and E) but also occurred in its absence (Fig 6B), a Q I was again recorded more often when there was no infarction

Deep inspiration decreased the size of Q III in most patients with infarction and in normal controls

(Fig 5 and 6)   Infrequently Q III was abolished by deep breathing in subjects without infarction (Fig 5C and 6B)   In infarction Q I was usually absent or small   If in individual patients Q I was shown before infarction, it was reduced in amplitude or abolished after the attack (Fig 3)   but when the cardiograms of all patients with posterior infarction were examined Q I was found in 14 out of 40 records   The presence or absence of Q I was, therefore, of no diagnostic significance
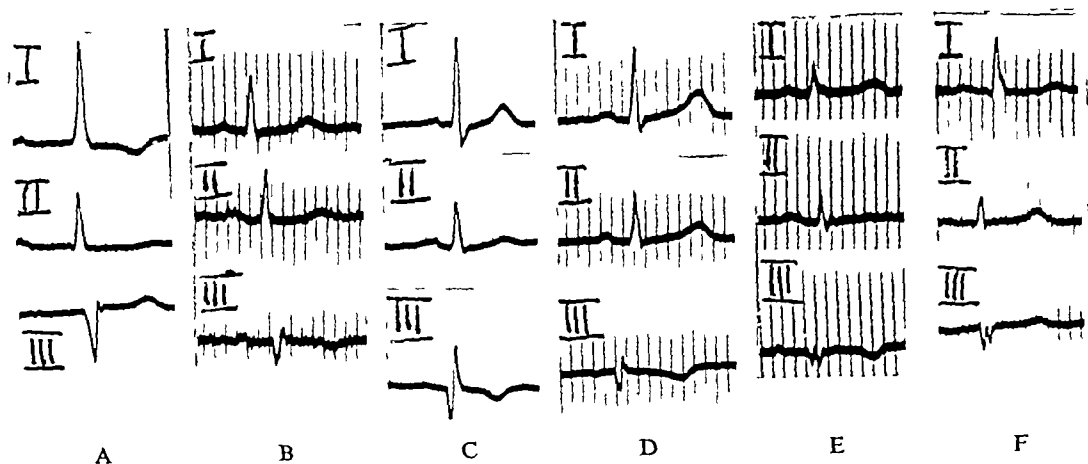
FIG 2 —Electrocardiograms of the discordant type with equivocal Q deflections

(A) Case 9   Man aged 67   hypertension and posterior infarction (ten years after the tracing shown in Fig 3A)
(B) Case 10   Man aged 50   left mammary pain
(C) Case 11   Woman aged 65   moderate hypertension

(D) Case 12   Woman aged 37   extrasystoles
(E) Case 13   Man aged 66   posterior infarction (one year after the tracing shown in Fig 3H)
(F) Case 14   Woman aged 44   left mammary pain

II UNIPOLAR LIMB LEADS IN POSTERIOR CARDIAC INFARCTION

Unipolar limb leads were analysed in 18 cases of posterior infarction   The leads were taken with the Wilson technique and then designated VR, VL, VF   In other cases, the Goldberger method was adapted to the central terminal of Wilson by detaching the indifferent limb electrode from the limb under exploration, the leads were then called aVR, aVL, and aVF   The left leg lead showed a deep and wide Q (with an amplitude of 30 per cent or more of the amplitude of R in this lead and with a width of 0 04 second or more) when Q II and Q III were also characteristic (Fig 4)   In cardiograms with discordant standard leads and equivocal Q waves, Q in the left leg lead was wide (Fig 6A), but not always deep (Fig 6D), in records of the concordant type with small Q waves in lead II and III, Q in the left leg lead was also small in width and size (Fig 5A and D)   In all cases of infarction, the Q wave whatever its size, was deeper in lead III than in the left leg when allowance was made for augmentation in Goldberger leads   The voltage of Q in the left leg lead was reduced by deep inspiration

All cases of posterior infarction showed an initial upright deflection in the left arm lead, it was more than 1 mm in amplitude and often broad or slurred in the ascending limb   A monophasic upright deflection was recorded in some cases, others showed an S wave, but a small R followed by a deep S was not

seen   In the right arm lead, the initial deflection was upright in 15 out of 18 cases and varied in amplitude from a small spike to a size of 4 mm , an R wave in the right arm would be expected to show as a Q wave in lead I, but in all 15 cases Q I was either absent or smaller than R in the right arm lead after allowance was made for augmentation   When right bundle branch block was added to posterior infarction, the unipolar limb leads conformed to the infarction pattern (Fig 4D)

III UNIPOLAR LIMB LEADS IN PATIENTS WITHOUT INFARCTION SHOWING CARDIOGRAMS WITH INCONCLUSIVE Q WAVES IN THE STANDARD LEADS

Equivocal Q waves in the standard leads did not signify infarction if the initial deflection in the left leg lead was upright (Fig 5C and 6B), in patients of this type, Q III was abolished by deep inspiration   In concordant cardiograms, a small Q in the left leg lead was as inconclusive as a small Q in lead II and III, it was not abolished by deep inspiration   Unlike the Q of infarction, Q VF was often of the same size as Q III (Fig 5E and F)   In these cases, the left arm lead also differed from the infarction pattern and showed an R wave of small voltage   If Q II and Q III were equivocal and the cardiogram conformed to the infarction pattern in lead VF and VL, a significant deviation might yet be shown in the relation of Q I to the right arm lead   in this case, Q I was of the same size as R in VR (Fig 5B)   In
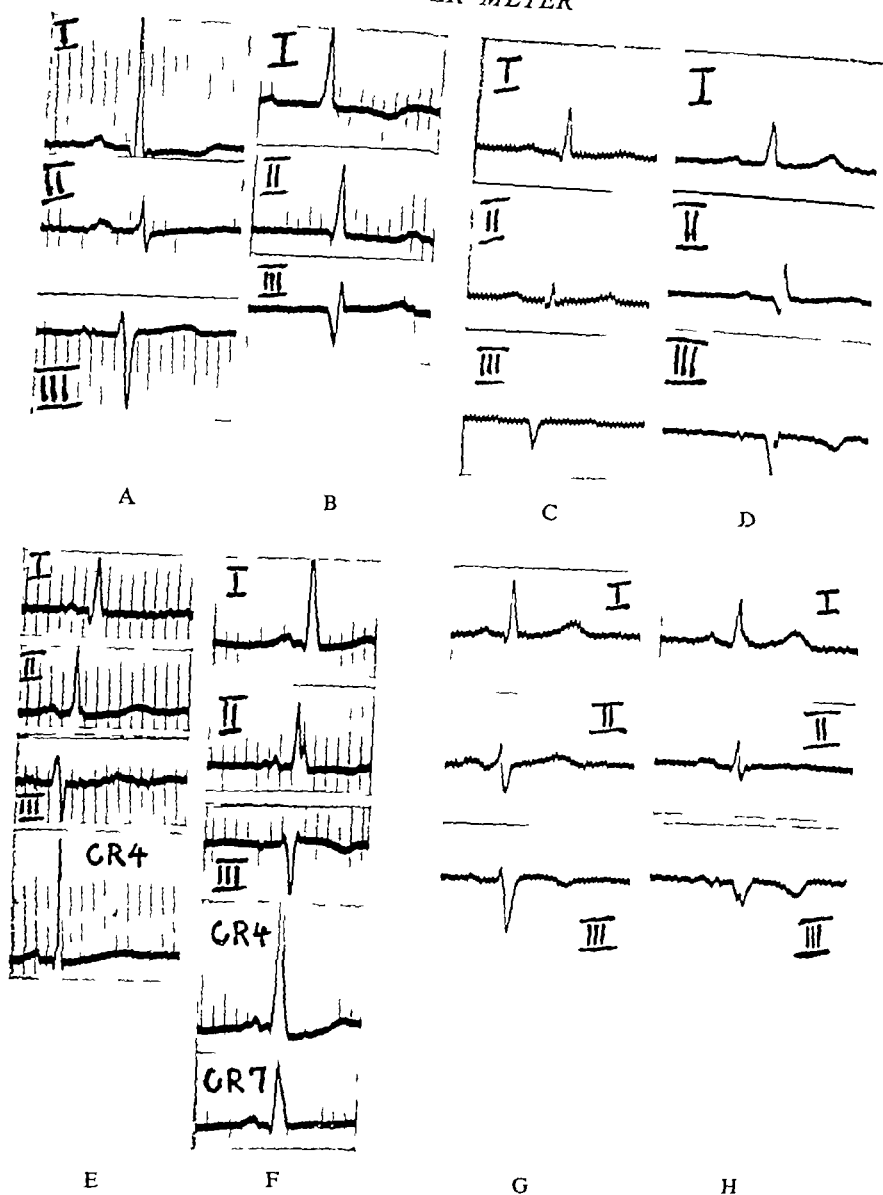
FIG 3.—Electrocardiograms taken before and after posterior infarction

(A) Case 9   Man aged 57   hypertension
(B) The same   two years after infarction
(C) Case 15   Man aged 58   angina of effort
(D) The same   three weeks after infarction

(E) Case 16   Woman aged 67   hypertension
(F) The same   on day of infarction
(G) Case 13   Man aged 65   angina of effort
(H) The same   two months after infarction

discordant cardiograms, Q in the left leg lead was less wide than the Q of infarction, it differed from the Q VF seen in the concordant type of tracing in that it was deep yet smaller than Q III, even in the absence of infarction   An initial downward

deflection in the left arm lead occurred only in patients without an infarct (Fig 6E)

It was concluded that equivocal Q waves in the standard leads did not indicate posterior infarction if in unipolar limb leads the initial deflection was
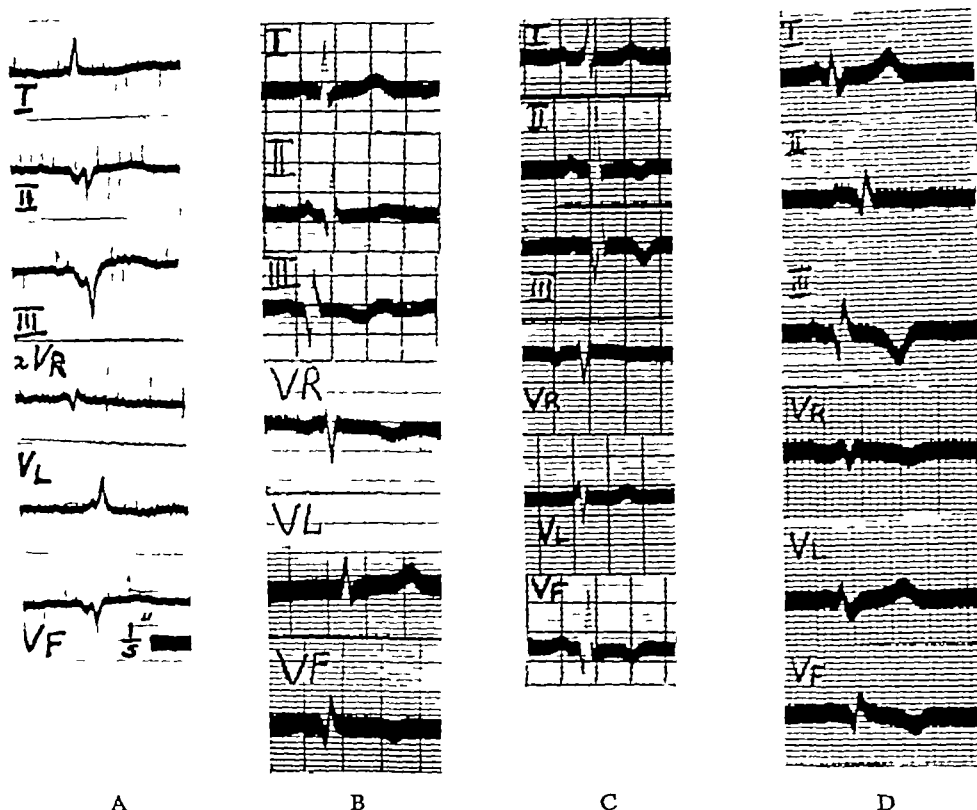
FIG 4 —Unipolar limb leads in cardiograms with characteristic changes in the standard leads

(A) Case 17 Man aged 61 infarction three years ago

(B) Case 18 Woman aged 39 infarction two years ago

(C) Case 1 Man aged 45 infarction three weeks ago (10 days after the tracing shown in Fig. 1A)

(D) Case 19 Man aged 54 infarction nine weeks ago

upright in the left leg, or downward in the left arm, or if an initial R shown in the right arm was also recorded in lead I as a Q of similar size, a Q in the left leg did not represent infarction if it was of the same amplitude as Q III   When the standard leads were concordant, equivocal Q waves in lead II and III were suggestive of infarction if Q in the left leg lead was smaller than Q III and the right and left arm leads conformed to the infarction pattern   In discordant tracings, care had to be taken to ascertain that the downward deflection in lead III was a Q and not an S wave   A true Q III stood for infarction if Q in the left leg lead was 0 04 second or more in width   a deep Q, even when smaller than Q III, did not indicate an infarct in this type of tracing   If Q III was abolished by deep inspiration, absence of Q in lead VF could be inferred and infarction was unlikely, the effect of deep inspiration was inconclusive if it left Q III unchanged or reduced in size

DISCUSSION

The preceding observations have shown the unipolar limb leads to be of value in the cardiographic diagnosis of posterior infarction   In the past, the unipolar left leg lead was singled out for examination in cases of posterior infarction, and the diagnostic significance of deep and wide Q deflections in this lead was stressed (Myers and Oren, 1945, Goldberger, 1947)   Although such Q deflections were found in the present series of cases, difficulties arose because there were patients with infarction who exhibited a small and short Q, and subjects without infarction with deep Q waves in lead VF   When such equivocal cardiograms were studied, examination of the other unipolar limb leads was valuable

On theoretical grounds, changes in the curves of the left and right arm must be expected with the development of a Q in the left leg lead due to
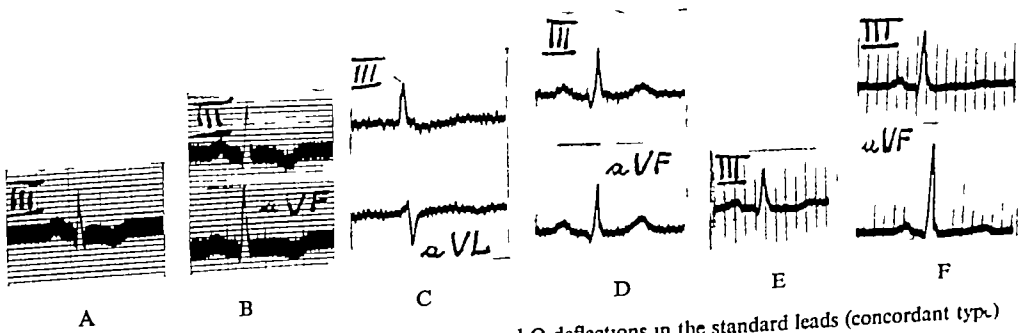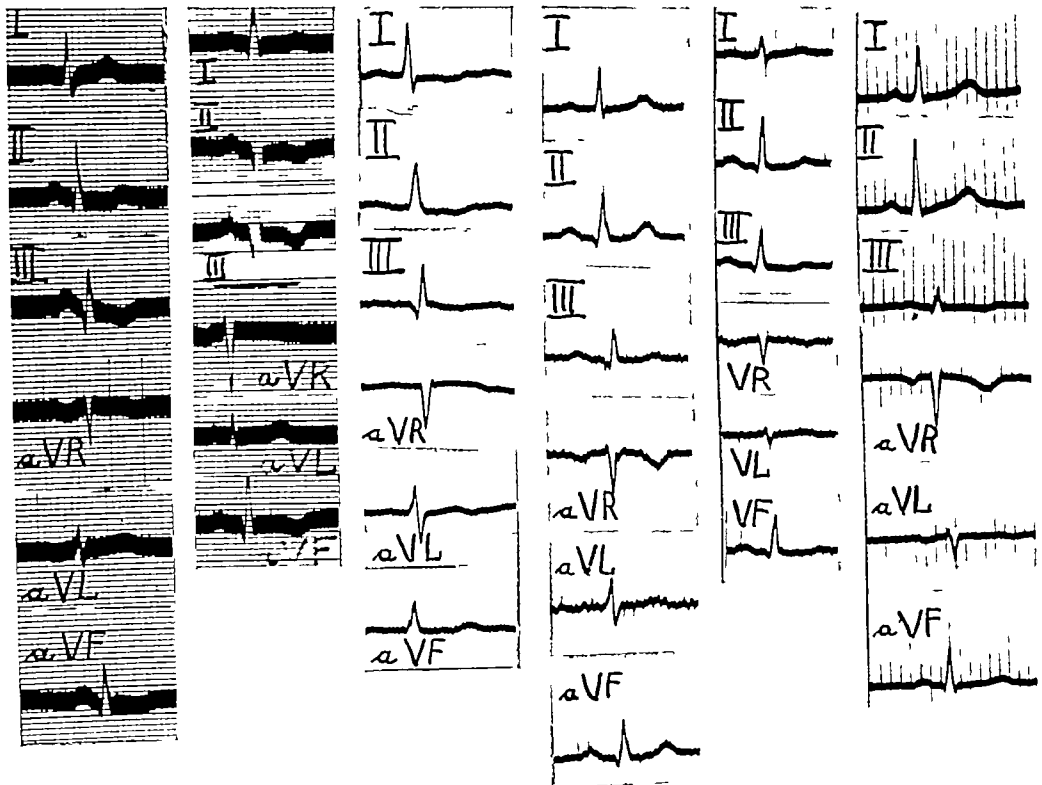
FIG 5 —Unipolar leads in cardiograms with equivocal Q deflections in the standard leads (concordant type)

Lower row   Leads taken on deep inspiration

(A) Case 20   Man aged 49   infarction nine months ago
(B) Case 21   Man aged 38   repetitive paroxysmal tachycardia
(C) Case 22   Woman aged 36   mitral stenosis, aortic incompetence, auricular fibrillation

(D) Case 23   Man aged 53   infarction one year ago
(E) Case 24   Man aged 64   emphysema and bronchitis
(F) Case 25   Woman aged 47   hypertension
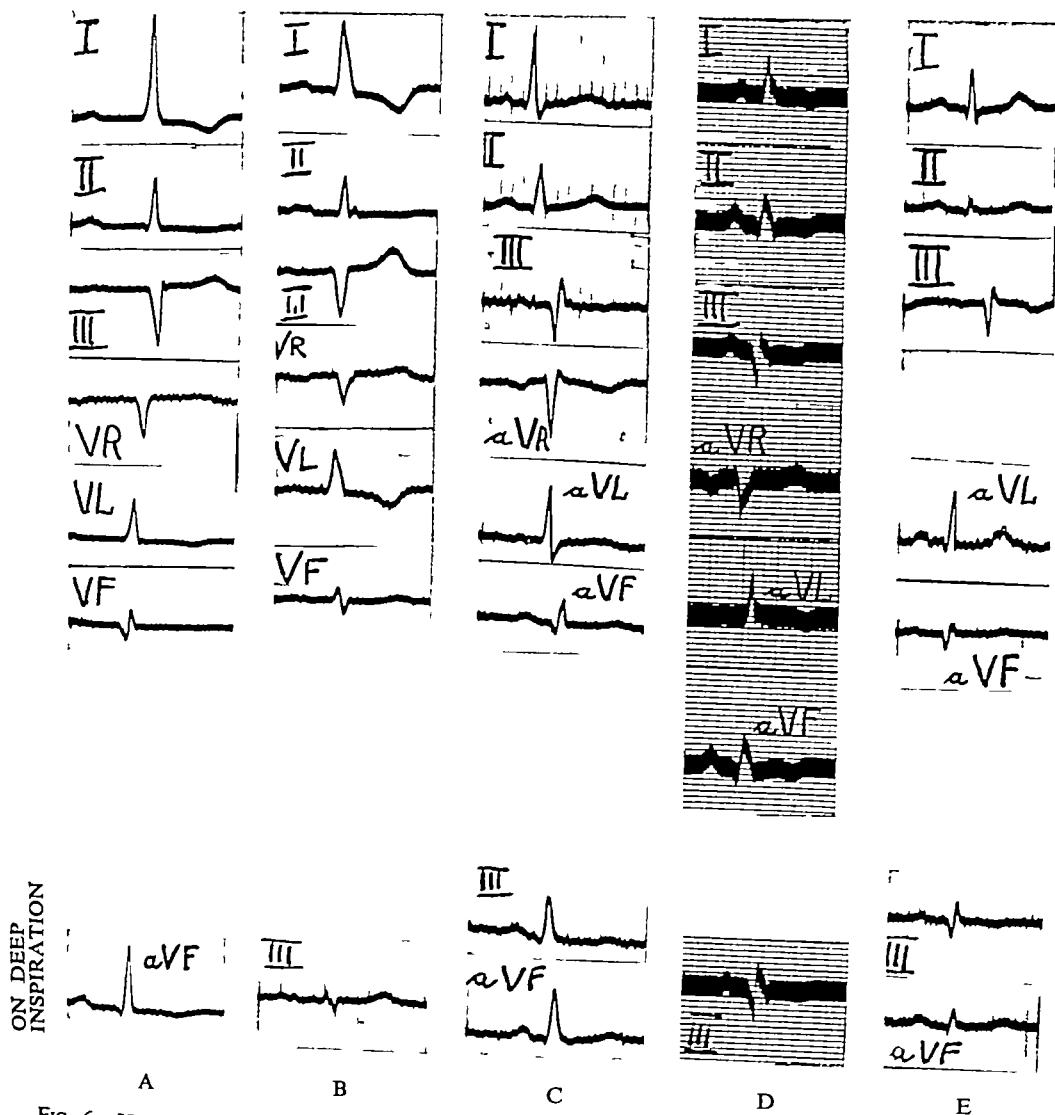
FIG 6—Unipolar leads in cardiograms with equivocal Q deflections in the standard leads (discordant type)

Lower row   Leads taken on deep inspiration

(A) Case 9   Man aged 57   hypertension and posterior infarction (see also Fig 2A, 3A and B)
(B) Case 26   Man aged 63   hypertension
(C) Case 27   Man aged 57   hypertension

(D) Case 28   Man aged 49   infarction four weeks ago
(E) Case 29   Woman aged 69   moderate hypertension

infarction as the sum of the potentials in the three limbs leads must remain zero at any given time Examination of the standard leads had shown that a Q I present before infarction is reduced in size or abolished by the infarct, since such Q waves usually derive from an initial negative deflection in the left arm lead, it was expected that the development of early negativity in the left leg lead from infarction would cause early positivity in the left arm lead, and this has been confirmed by observation   As the upward deflection in the left arm lead is a counterpart of Q in the left leg lead, it follows that it must occur early in ventricular excitation and be synchronous with Q in the left leg lead   Lead I

measures the potential difference from the left to the right arm, a Q in the left arm or an R in the right arm will be recorded as a Q in lead I Since early negativity in the left arm does not occur in these cases of posterior infarction, a Q in lead I can only be due to early positivity in the right arm, but the positive deflection in the left arm must partly or wholly counteract the formation of a Q in lead I from the positive deflection in the right arm, therefore, Q I is smaller than R in V R, or it is absent Observation has confirmed this argument In the absence of infarction, a Q in the left leg lead is not necessarily combined with a prominent R in the left arm lead the initial deflection may be of low voltage (Fig 5E and F) or may be directed downward (Fig 6E) There is also the possibility that R in the left arm lead may not occur early in ventricular excitation this can be recognized if the R wave does not interfere with the formation of a Q I from R in the right arm lead Such a combination of events has been seen in one record (Fig 5B)

When the standard leads are concordant, infarction is likely if Q III is larger than Q in the left leg lead This is an indirect method of observing the early upright deflection in the left arm which reinforces the downward direction of Q III initiated by Q in the left leg, in the absence of infarction, the small amplitude of R in the left arm prevents this reinforcement of Q III Discordant cardiograms usually show a prominent R in the left arm lead, hence Q III is larger than Q in VF also in the absence of infarction Deep inspiration, by causing a shift of the long axis of the heart away from the left arm, reduces the amplitude of R in VL (Fig 5C), it therefore abolishes the Q waves which are not due to a Q in the left leg lead

In the left leg lead, a Q of infarction may be small in size and duration in concordant tracings It is wide though not necessarily deep in cardiograms of the discordant type, when a wide and deep Q III is also shown, but a wide and deep Q in lead III alone does not stand for infarction because it also occurs from left ventricular hypertrophy (Myers and Oren (1945), also Fig 6B)

Summary and Conclusion

The electrocardiograms of 40 patients with posterior infarction were examined for modifications of the QRS complex indicating infarction, there were 7 cases with inconclusive Q waves in lead III, or II and III, and they closely resembled cardiograms from subjects without infarction In concordant tracings, uncertainty was caused by small Q waves in leads II and III, in the discordant type, difficulties arose when Q was deep, or wide and deep, in lead III, and small or absent in lead II, care had to be taken to examine each beat in lead III to ascertain that the downward deflection in this lead was not in fact an S wave A Q wave in lead I was more often seen in normal subjects than after infarction, but this was of no diagnostic significance, in the individual patient, such a Q wave shown before infarction was reduced in amplitude or abolished by the infarct

Unipolar limb leads were examined in 18 cases of posterior infarction with Q waves in the standard leads The left leg lead showed a Q deflection in all cardiograms, it was deep and wide if typical Q waves were seen in leads II and III When the standard leads were discordant with a wide and deep Q III, Q in the left leg lead was wide, but not always deep When the standard leads were concordant with inconclusive Q waves in leads II and III, Q was also small in the left leg In all records of plain posterior infarction, Q III was larger than Q in the left leg, the left arm lead showed an initial upright deflection of more than 1 mm, in most, but not all records, an initial upright deflection was also shown in the right arm, and this did not appear as a Q wave of the same size in lead I

From an examination of unipolar limb leads in subjects without infarction it was concluded that equivocal Q waves in the standard leads did not indicate plain posterior infarction if the initial deflection was upright in the left leg, or downward in the left arm, or if an initial R shown in the right arm was also recorded in lead I as a Q of similar size A Q wave in the left leg lead did not represent infarction if it was of the same amplitude as Q III When the standard leads were concordant, equivocal Q waves in leads II and III were suggestive of infarction if Q in the left leg lead was smaller than Q III and if right and left arm leads conformed to the infarction pattern In discordant tracings, the width of the Q wave in the left leg lead was significant, a deep Q wave, even when smaller than Q III, did not indicate an infarct The effect of deep inspiration on the Q wave in lead III and lead VF was also examined, if Q III was abolished by deep inspiration, absence of Q in lead VF could be inferred

In the discussion the electrical events leading to the observed cardiographic patterns were analysed

I wish to record my gratitude to Dr William Evans for much advice and encouragement received from him

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TRANSPOSITION OF THE AORTA AND PULMONARY ARTERY DEMONSTRATED BY ANGIOCARDIOGRAPHY

BY

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Complete transposition of the great vessels is one of the less common congenital anomalies Survival after birth is dependent upon the presence of some communication between the right and left sides of the heart that will permit crossing of the greater and lesser circulations and enable venous blood to reach the lungs

The case described below is of particular interest because of the absence of diagnostic criteria afforded by the usual methods of clinical and radiological examination

CASE REPORT

D T, aged 5 years, had been cyanosed since birth He became very breathless on the slightest exertion and he frequently assumed the squatting position There was no history of rubella during the mother's pregnancy

Physical examination The child was undersized, with marked cyanosis which was of equal intensity in both the upper and lower extremities There was dyspnœa at rest and marked clubbing of the fingers and toes Examination of the cardiovascular system showed bulging of the præcordium and slight general cardiac enlargement A harsh systolic murmur was heard down the left side of the sternum, and there was a pure pulmonary second sound There was no thrill and no diastolic murmur The femoral pulses and blood pressure were normal, and the lungs were clear

The blood count showed a considerable degree of polycythæmia The figures with the normal values at the age of 5 years for comparison were as follows hæmoglobin 21 grams (12 6), red blood corpuscles 7 9 million per c mm (4 6), leucocytes 12,000 per c mm, mean corpuscular diameter

7 3μ (7 4), packed cell volume 63 per cent (37) mean corpuscular volume 80 c μ (80), mean corpuscular hæmoglobin concentration 33 per cent (34)

Cardiography, using augmented unipolar leads in addition to standard leads, was performed and has been interpreted according to the criteria of Goldberger (1947) (Fig 1) The standard limb leads show high voltage complexes and marked right axis deviation The P waves in leads I and II and VF are of increased amplitude and duration (lead I, duration 0 11 sec, height 2 mm, lead II, duration 0 12 sec, height 3 mm, lead VF, duration 0 11 sec, height 2 5 mm) The heart is vertical in position, since the unipolar left leg lead resembles lead V6 and therefore faces the epicardial surface of the left ventricle There is also clockwise rotation of the heart round its long axis, because the unipolar left arm lead faces the cavity of the right ventricle VL shows a small R wave and a large S wave and a negative T wave and the præcordial leads show RS patterns

There is no definite evidence of right ventricular strain, but this may be deduced from the presence of auricular hypertrophy Goldberger states that if any of the unipolar extremity leads show P waves with duration of 0 11 sec or more and an amplitude of 2 5 mm or more, auricular hypertrophy may be suspected

Radiography A postero-anterior radiogram of the chest showed an enlarged heart with a prominent pulmonary conus and full root shadows, the lung fields showed congestive changes (Fig 3)

Fluoroscopy and barium swallow revealed an enlarged heart, with an enlarged pulmonary conus, and very dilated pulmonary vessels with marked pulsation The aorta appeared to be dextroposed
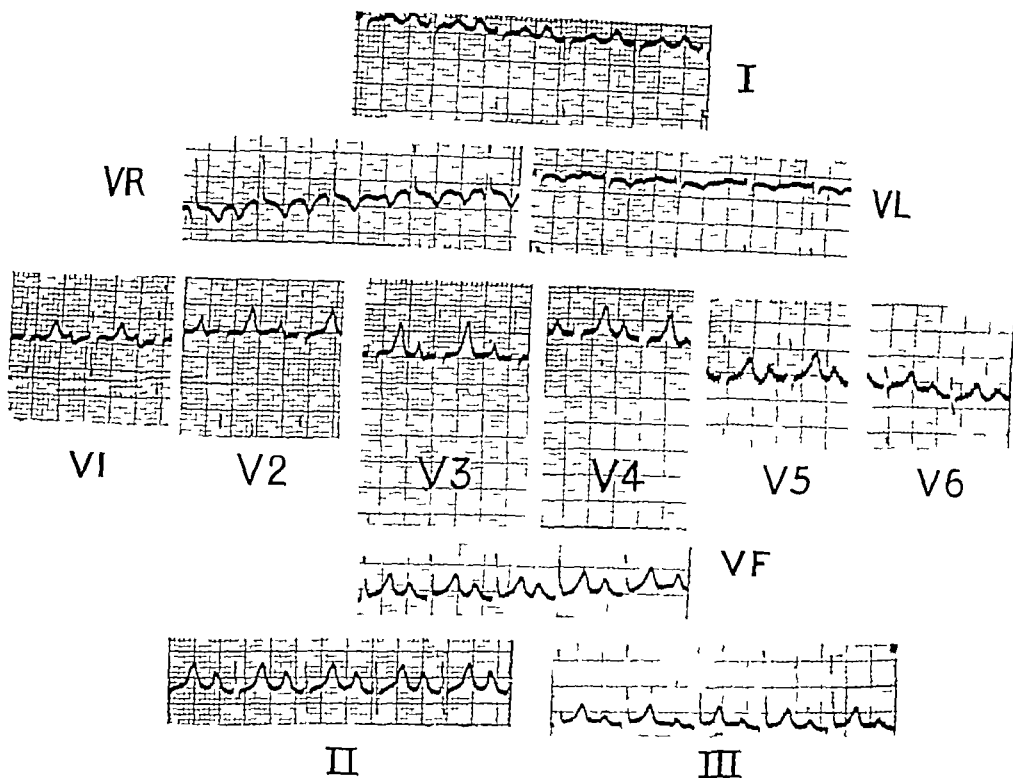
279

FIG 1 —Standard and unipolar lead electrocardiograms   The heart is vertical with clockwise rotation round
  its long axis   Right auricular strain and indirect evidence of right ventricular strain are present
            Limb lead 1 mv = 1 cm   Præcordial leads 1 mv = 1 5 cm

ANGIOCARDIOGRAPHY

Technique   Angiocardiography was carried out
under general anæsthesia   Two injections of 40 ml
70 per cent pyelosil were made into the antecubital
vein of the right arm   In the first instance the
patient was X-rayed in the right posterior oblique
position lying supine, and in the second instance in
the antero-posterior position lying on his side

A rotating serial cassette changer was used with
the following radiographic factors   200 M A
72–74 K V P , 1/20th second exposure, at a target
film distance of 36 inches   In both antero posterior
and oblique positions six exposures were made at
one-second intervals starting at one second after
the injection

Oblique radiograms   On the two-second film
(Fig 3) good filling of the superior vena cava
will be noted   The right auricle is clearly out-
lined and the reflux of contrast medium into the
inferior vena cava is seen   The right ventricle is
filled and enlarged and the interventricular septum

is convex posteriorly   The ascending aorta and
arch are outlined and a faint trace of contrast
medium is visible in the left side of the heart just
posterior to the right auricle   The pulmonary
artery is outlined very faintly

On the three-second film (Fig 4) the right auricle
is still outlined and the ventricle is more clearly
shown, as well as the ascending aorta   aortic
arch, and descending aorta   The innominate and
external and internal carotid arteries are also out-
lined   The left auricle and ventricle are fairly well
delineated and the pulmonary artery can now be
seen clearly demonstrated as a second arch below
the aorta   *On the subsequent films* most of the
contrast medium is seen scattered throughout the
pulmonary vascular bed and the cardiac chambers
are not clearly differentiated

*Antero-posterior radiograms   In the two-second
film* (Fig 5A and B) the right auricle and ventricle
are clearly demonstrated   The ascending aorta
is seen to arise from the right ventricle   The

FIG 2 —Postero-anterior 6-ft film of the chest

innominate artery, the right carotid and the internal carotid arteries are shown and some contrast medium has entered the left ventricle *On the three-second film* (Fig 6) the left side of the heart is now filled with contrast medium The aorta is still shown the pulmonary artery and the main pulmonary branches are partly demonstrated As in the case of the oblique radiograms subsequent films did not reveal any details of the cardiac chambers as most of the contrast medium had entered the pulmonary vascular bed and partly left the heart

The radiographic examination quite clearly demonstrated the transposition of the aorta and pulmonary artery The septal defect itself is not shown, but the rapid filling of the left side of the heart on the two- and three-second films is very suggestive of the presence of such a defect It is

A

B

FIG 3 —Angiocardiogram at 2 seconds   Patient in the right posterior oblique position   The right auricle and
ventricle are demonstrated as well as the pulmonary artery and aorta
(B) (Inset) Diagram of Fig 4A   S V C =Superior vena cava   L A —Left auricle
                                 I V C =Inferior vena cava   P A =Pulmonary artery
                                 R A =Right auricle   Ao =Aorta
                                 R V =Right ventricle

FIG 4—Angiocardiogram of the patient in the oblique position taken at 3 seconds   Pulmonary artery and aorta are clearly demonstrated

(B) (Inset)   S V C =Superior vena cava   P A =Pulmonary artery
              R A =Right auricle   L A =Left auricle
              R V =Right ventricle   Ao =Aorta

B   A

FIG 5 —Angiocardiogram at 2 seconds of the patient in the antero posterior position   Right auricle and
ventricle are clearly demonstrated   The aorta is seen to rise from the right ventricle

(B) (Inset)   S V C =Superior vena cava
               R A   =Right auricle
               R V   =Right ventricle
               L V   =Left ventricle
               Ao   =Aorta
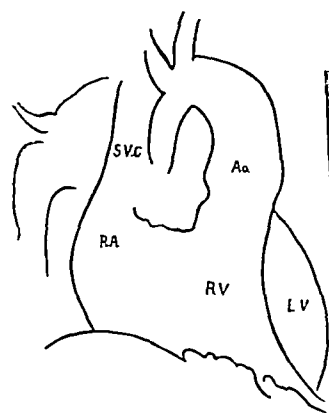
B

A

F$_{IG}$ 6—Angiocardiogram, at 3 seconds, of the patient in the antero-posterior position The right ventricle, aorta and the left ventricle are outlined

(B) (Inset)   S V C =Superior vena cava
R.A   =Right auricle
R V   =Right ventricle
L V   =Left ventricle
Ao   =Aorta

impossible to decide if this defect is auricular or ventricular

Cardiac catheterization was not undertaken as it was felt that it would yield no further useful information

DIFFERENTIAL DIAGNOSIS

The history of cyanosis from birth and the physical signs in this case suggested either transposition of the aorta and pulmonary artery with an associated widely patent septum, tricuspid atresia, single ventricle, or Fallot's tetrad with extreme pulmonary stenosis   Electrocardiography did not reveal the gross right or left heart strain that would have been expected in pulmonary and tricuspid atresia respectively   Taussig (1945) describes a characteristic cardiac contour on fluoroscopic examination in cases of transposition of the great vessels   Since the aorta lies further to the right and in front and the pulmonary artery further to the left and behind, the shadow at the base of the heart is the reverse of normal, being wider in the left anterior oblique view and narrower in the antero-posterior view   In the latter position the shadow of the pulmonary conus is usually absent and a rhythmical change in size of the right auricle and ventricle, due to frequent reversal of the shunt, is seen   In our case no such distinctive contour or rhythmical alteration was observed, and a pulsating shadow noted in the region of the pulmonary conus was proved by angiocardiography to be the aorta

DISCUSSION

Complete transposition of the aorta and pulmonary artery may be accompanied by patencies of the normal foetal pathways the foramen ovale, and the ductus arteriosus, or by additional septal defects   As Taussig (1947) points out the larger the communication between the two sides of the heart, the longer will be the period of survival When the ductus arteriosus or foramen ovale alone are patent, survival for more than a few hours or days does not occur, but infants who in addition have widely patent interventricular septa may survive for much longer   Taussig considers that even in cases where both septa are widely patent survival is rarely possible beyond the age of eighteen months   Hanlon and Blalock (1948) collected 123 cases of complete transposition with associated abnormalities and found the average duration of life was nineteen months   Six patients lived ten years or longer, but the average age at death in the other 117 patients was five and a half months Twelve cases had an interventricular septal defect without other abnormalities and these patients lived for a mean period of four years and one month   The association of a patent foramen ovale with patent interventricular septum (19 cases) increased the survival to four years nine months, but the association of other defects decreased the duration of life   Of Kato's (1930) 86 cases 16 had defects of both septa, the average survival time of these 16 being five and a half years   But the inclusion of 2 patients aged nineteen and fifty-six years respectively among these 16 cases presents a falsely optimistic picture   It appears therefore that complete transposition is unlikely to be compatible with survival after the age of four years, even when a patent interventricular septum is present

SUMMARY

A case of complete transposition of the aorta and pulmonary artery is described in a child five years of age showing intense cyanosis and great breathlessness on exertion   The condition was clearly revealed by angiocardiography and could not have been detected by the usual clinical and radiological methods   A survey of the literature shows that survival beyond the age of four and a half years is very rare in this condition

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THE RESULTS OF MEDICAL AND SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION

BY

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For a variety of reasons it is difficult to evaluate the influence of therapeutic procedures in essential hypertension, the peculiar feature of which is an elevation of the diastolic blood pressure   Patients present individual problems and do not readily adapt themselves to precise categories and strict comparisons   Furthermore, while hypertension commonly runs a prolonged course over the years and shows of itself spontaneous fluctuations from day to day, yet for reasons unknown the intensity of the disease may abruptly increase and the pace towards a fatal termination quicken with unexpected suddenness   We have no measure of vascular vulnerability with which to compare one patient with another

A feature of the disease, even in the same subject, is its variability   Symptoms pass through phases of activity and seldom correlate with the blood pressure readings   Arteriolar tone is not a fixed quantity   The diastolic pressure is constantly changing, occasionally falling to surprisingly low levels for no obvious reasons   It is remarkable how, after many months of intermittent disablement by headache or giddiness in middle life, a symptom-free stage may ultimately be attained in later years without, however, much significant alteration in the blood pressure   These natural variations and remissions hinder reliable therapeutic deductions in the individual patient   Nervous and emotional factors are difficult to assess and it is well recognized that the hypertensive patient is highly susceptible to suggestion—*particularly when it is reinforced by the sympathetic care and understanding of an enthusiastic adviser*   Psychological factors may distort the picture and obscure the basic facts

By the study of a group of patients over a sufficiently long period the fallacies attributable to the inconsequential fluctuations of pressure and spontaneous remissions in symptoms are minimized to some extent   All our patients were under the care and supervision of the same observers   accustomed to the same surroundings, the same methods of clinical investigation and familiar with the ways of the examiners, they were thereby exposed to few extraneous factors liable to influence their nervous tension adversely   By the adoption of an attitude of benevolent neutrality, psychological influences were kept as uniform as possible from patient to patient   Each patient reported at intervals and was assessed by the same observers

Many attempts have been made to judge the efficacy of the surgical attack on hypertension (Adson *et al*, 1934, 1936, Allen and Adson, 1940, Smithwick, 1940, 1944, and Grimson, 1947)   Inadequate standards for comparison have proved a stumbling-block   Not infrequently an author has assembled two groups for comparison, one medically and the other surgically treated   To some extent the conclusions are invalidated by a comparison of the author's series of surgically treated patients with a medical group investigated by someone else necessarily employing slightly different standards, techniques, and methods   For example, Wagener and Keith (1939) report on a series of medically treated patients with hypertension and their results have been used by several surgical authors for comparison with their own cases, Flaxman (1944) describes a medical series of his own compared with the surgical experiences of Peet *et al* (1940), Hammarström (1947) compares his surgical cases with a series of non-operated cases described by Bechgaard (1946), and so on   The general consensus of opinion is that sympathectomy is of value particularly in younger patients before the development of serious coronary or renal disease

* Working under the tenure of a Scholarship awarded by the Grocers' Company of London.

Hammarstrom (1949) believes that in the severer cases with retinal exudation life expectancy is increased in a sympathectomized group as compared with similar patients treated by medical means

THE PROBLEM

The problem under consideration is the evaluation of the results obtained by medical and surgical means in the treatment of essential diastolic hypertension This has involved a review of the progress of a large number of patients of whom some were surgically and some medically treated The results are considered in general as well as in certain particular details In the investigations now to be described, both ' medical " and " surgical ' groups have been examined and assessed by the same doctors, thus ensuring, it is hoped, more constant standards of comparison and hence more accurate conclusions Surgery was first employed by us nine years ago All the cases subsequently sympathectomized have been followed-up and form the basis of the present study The control medical group dates back to five years ago

THE MATERIAL

The material on which our investigations are based consists of 151 cases of essential hypertension of whom 96 were treated by medical measures and 55 by surgery

The investigations common to all the patients started on their admission to hospital In general arteriosclerosis, angina, congestive heart failure, poor renal function, and an age in excess of 50 years, with few exceptions, were usually regarded as contra-indications to surgical intervention, but minor cerebral episodes, even transient hemiplegias, did not exclude the possibility of surgical help Changing standards of selection for surgery have proved of help to us in the construction of the two groups —surgical and medical—for the purposes of the present analysis of the results obtained

When surgery was not employed the medical measures recommended were those in common use, including in the first instance a rest in bed in the hospital for two or three weeks, and thereafter some limitations in activities a reduction in body-weight when necessary, the administration of simple sedatives such as phenobarbitone and analgesics from time to time, the use of the head-up bed for the prevention of morning headache, and vene-section very occasionally Most emphasis was put on reduced activities and the avoidance of fatigue In the surgical group Smithwick s (1940) method of lumbo-dorsal sympathectomy was employed in 75 per cent of the 55 patients and lumbar sympathectomy in the remainder treated several years earlier

The medically treated group of 96 cases consisted of 76 benign (that is with retinal changes less than papilloedema) and 20 malignant cases (that is with papilloedema accompanied or unaccompanied by other retinal changes), the surgically treated group of 55 was composed of 45 benign and 10 malignant cases

The ' benign medical " group consisted of 76 cases, 17 males and 59 females, varying in age from 30 to 71, the average age being 47 years, the dura tion of the follow-up period varied from six months to five years The ' benign surgical " group was composed of 45 cases, 18 males and 27 females, varying in age from 19 to 60, the average age being 40 years, the follow-up periods varied from three months to eight and a half years

The ' malignant medical ' group contained 20 cases, 14 males and 6 females, varying in age from 31 to 66, the average age being 50 years, the follow up periods ranged from one month to one year The ' malignant surgical ' group was composed of 10 cases, 5 males and 5 females, whose ages ranged from 36 to 61, the average age being 46 years Follow up periods varied from three months to three years

METHOD OF INVESTIGATION

Assessment of patients before and after treatment The same routine of tests and investigations was applied to every patient in the series before treat ment and at intervals after treatment The methods employed consisted of a careful history to exclude any primary renal disease, endocrine disorder or other cause for the hypertension Particular atten tion was devoted to a routine physical examination with special note of the following points

(1) Assessment of retinal grade according to the method of Wagener and Keith (1939) into four classes—1, 2 3, and 4 (Normal is graded 0, papilloedema is graded 4)

(2) Assessment of cardiac efficiency graded according to the following method A normal B, slight impairment during exertion C, consider able impairment during exertion and D impair-ment at rest

(3) Assessment of renal efficiency, according to results of the urea concentration range (Cameron 1934) or the urea clearance tests (Peters and Van Slyke 1946) thus A, very good, B, good C fair, and D, poor

(4) Assessment of severity of symptoms thus A, symptom free B moderate symptoms but fit for work, C, severe symptoms, unfit for work and D, dead

(5) Assessment of the diastolic pressure As a measure of the peripheral resistance the diastolic

pressure is recognized as a more reliable indication of the severity of the hypertensive process than the systolic level Furthermore, the diastolic pressure has a smaller range_of fluctuation than the systolic and is less susceptible to unpredictable excursions For comparative purposes the diastolic pressure therefore yields the more reliable figure and we have made use of it in our assessment The basic figures were taken when the patient, already thoroughly familiar with the method, had rested for at least 10 to 15 minutes recumbent on a couch It must be realized that this reading was not taken until the end of the examination, by which time it was ensured that the patient was adjusted to his surroundings and completely at ease in a quiet restful room with which he was familiar The diastolic pressure is recorded in mm of mercury for each patient and not graded A, B, C, or D as for the other observations listed above

During the clinical examination note was made of the physique and nutrition of the patient, the pattern of the electrocardiogram, and the heart-size measured radiologically by the method of Unger-leider and Gubner (1942) These latter observations however, had not all been made in every case before treatment, and therefore were discarded in the statistical analysis of the results

The construction of matched groups for comparison of results The second part of the investigation consisted in dividing the patients into matched groups for the purpose of comparing the results of the two methods of treatment As the hypertensive process as a rule runs a milder course in the female (Bechgaard 1946, Rogers and Palmer, 1946–7) the surgical cases were divided on a sex basis Each of these male and female groups was subdivided into smaller groups composed as far as possible of persons of similar ages and with similar grading in the tests listed above This procedure resulted in the surgical cases being divided into 11 female and 8 male groups, as shown in Table I

Next each 'medical' patient's results were carefully scrutinized and he was placed in a medical group corresponding to the 'surgical' group whose criteria he best fitted Those medical cases who fitted exactly were termed "first-class comparisons , those who fitted well, but deviated in one degree in any criterion other than retinal grade were termed 'second-class comparisons", those who fitted less well, but better into that group than into any other were called 'third-class comparisons and were excluded from the statistical assessment of results

There now existed 8 male and 11 female groups each consisting of the original surgical cases and those medical cases that matched them, the matching

TABLE I

COMPOSITION OF GROUPS OF SURGICALLY TREATED PATIENTS

Group	Retinal grade	Cardiac efficiency grade	Renal efficiency grade
		Males	
1	0	A	A
2	I	A	A
3 A	II	A	A–B
3 B	II	B	A–B
4	III	C	C
5 A	IV	A	B
5 B	IV	C	C
5 C	IV	D	D
		Females	
1 A	0	A	A
1 B	0	A	B
1 C	0	B	A
2 A	I	A	A
2 B	I	A	B
2 C	I	C	C
3 A	II	A	A
3 B	II	C	A
4	III	A–B	C
5 A	IV	B	B
5 B	IV	C	C

being done on the basis of their pre-treatment investigations The addition of the medical cases as an "extension" to each surgical group caused no alteration in the description of any group as given in the above tables, since the third-class comparisons (which might have disturbed the homogeneity of a group) had been discarded The final constitution of each "surgical-plus-medical" group which are the units on which the actual work of comparison and statistical analysis was done is presented in Table II Amongst the males groups 1 to 4, inclusive and amongst the females groups 1A to 4, represent cases of benign hypertension. Malignant hypertension is composed of groups 5B and 5C male, and groups 5A and 5B female

Of the total of 23 male surgical cases, 18 were benign and 5 malignant, and of_the total of 27 medical cases used for the analysis (1st--2nd class) 13 were benign and 14 malignant Of the total of 32 female surgical cases, 27 were benign and 5 malignant, of the total of 47 female medical cases (1st class+2nd class comparisons) 42 were benign and 5 were malignant (Table II)

The third class comparisons numbered in all 22, 4 males and 18 females Of the 4 males, all were benign cases, of the 18 females, 17 were benign, and 1 malignant

It is customary to consider the adverse influence of obesity on the course of hypertension It has

TABLE II

Composition of the Matched Groups on which the Statistical Analysis is Based   The Third Class Comparisons are Discarded

Group	No of surgical cases	No of medical cases for comparison		
		1st class	2nd class	3rd class
Males				
1	3	3	—	—
2	5	1	2	—
3 A	6	1	1	—
3 B	2	2	1	3
4	2	2	—	1
5 A	3	4	3	—
5 B	1	2	—	—
5 C	1	1	4	—
Total	23	16	11	4
Females				
1 A	3	4	—	—
1 B	1	3	3	4
1 C	3	1	4	2
2 A	2	2	—	—
2 B	4	2	2	—
2 C	7	3	2	2
3 A	3	3	2	—
3 B	3	3	4	6
4	1	2	2	3
5 A	4	3	—	—
5 B	1	2	—	1
Total	32	28	19	18

been noted by many writers (e g Hunter and Rogers, 1923) that since an excess of body weight has an adverse bearing on the subject's expectation of life, it ought to operate even more severely to shorten the life span of the patient with hypertension Bechgaard (1946), however notes that contrary to expectation in his series of 1000 hypertensives which contained 311 obese patients, the latter had if any-thing a lower mortality than the others

In our small series there were 7 cases of obesity amongst the male surgical patients (5 benign and 2 malignant) and 4 amongst the male medically treated cases (3 benign and 1 malignant) In the females, of those surgically treated, 6 benign and 2 malignant were obese, whilst of the medical series, 19 were markedly overweight Obesity however had no relation to the mortality rate Of the 7 " medical " deaths in the benign group only one was an obese individual, the remainder were under average weight Of the 5 patients who died in the surgically treated group, 3 were under-weight and one average Obesity did not correlate with any significant deterioration in the course of the follow-up In fact in the most severe (malignant) hyper-

tensive cases, loss of weight was noted in 65 per cent of the medical and 30 per cent of the surgical cases and in the medical group it was an accompaniment of their rapid deterioration Body weight is therefore disregarded in our groupings

The adoption of matched groups is one which should meet Smithwick's (1948) requirements when he states " Further comparison of surgically and non-surgically treated cases divided into similar sub-groups in which the most important variables are held constant is desirable Until this can be done the influence and relative merits of various therapeutic measures upon the course of hyper-tensive vascular disease cannot be evaluated with certainty " Although the numbers in this investiga tion are small, our statistical colleague (B W) is satisfied that they are sufficiently large to provide information that is significant

STATISTICAL ANALYSIS

It must be emphasized strongly that the reliability of this analysis depends entirely on the validity of the grouping and matching of the cases described above In a clinical trial it is necessary that the allocation of cases to experimental and control groups shall be free from bias in respect of severity of symptoms, age, sex, or any other circumstance likely to have a bearing on prognosis This is usually contrived by a deliberately planned experi ment in which the cases are allotted to one or other form of treatment by a designed process In the present investigation, however, this was not done each patient was given surgical or medical treatment as seemed appropriate without strict regard to the possible future use of the cases in a statistical comparison

It has been possible, however, owing to such factors as changing standards as to indications for operation, patients declining operation, and so on, to match our surgical groups with medical, on the basis of the observations made during the patient s first stay in hospital and thus the series of cases has been converted retrospectively into a properly con trolled experiment to the best of our ability All the patients had been under detailed observation in the wards of the hospital and had submitted to the same routine

In the statistical analysis each group was taken separately and the " surgical ' cases compared with the 1st and 2nd class ' medical ' cases therein Six criteria are available for statistical evaluation These can be divided into two sections In the first these observations made at periodic re-examinations of those patients who survived are considered particularly in regard to the following factors (1) retinal grade, (2) cardiac efficiency, (3) renal

efficiency, (4) symptom grade, and (5) diastolic blood pressure The second part is a consideration of the incidence of deaths in relation to sex, severity of symptoms and method of treatment

COMPARISON BY SYMPTOMS AND SIGNS

In the analysis under this heading, the change was noted, for each patient, between the initial value or grade and that found at a specified time after treatment, in each of the items noted above The choice of the time interval is of some importance It is desirable to use as long a period as possible, to give ample time for the results of treatment to become manifest, a long interval also helps to reduce bias, by eliminating from the analysis all patients who die soon after the initial examination, and who therefore may have been too advanced in the disease to benefit from treatment It also serves to minimize any effects attributable to psychological betterment and unintentional suggestion On the other hand, increasing the time interval involves omission from the comparison of all the more recent cases The best compromise is to base the main comparison on the difference between the initial findings and those at the examination most nearly coinciding with the first anniversary of the commencement of treatment, or of sympathectomy

Data on change of symptom-grade are available for 47 surgical cases (20 male and 27 female) and 42 medical cases (11 male and 31 female), a total of 89 patients Observations on criteria 1, 2, 3, and 5 (see p 288) are also on record for most of these cases Comparisons of changes after three years were also made, but the number of cases was only 41, the findings for the one-year and three-year periods are fully concordant

Criteria 2, 3, and 4 are on the ABC scale, an arbitrary value of unity being given to each successive step Retinal grade is 0, 1, 2, 3, and 4, as described earlier, blood pressure differences were measured quantitatively in mm Hg In each group of patients the average change in the medically and surgically treated cases was calculated with respect to each criterion, and the probability that the observed difference, if any, might be attributable to chance fluctuations The combined probability that all the differences with respect to treatment might be chance effects were then calculated Where this probability is less than 1 20 the treatments are taken as giving significantly different results

Results of analysis The main findings are as follows

(1) In the *symptom grading*, the surgical cases show a great and decisive superiority over the medical The details for a 12-months interval are shown in Table III A positive value in the last

TABLE III
MEAN CHANGES IN SYMPTOM GRADE AFTER ONE YEAR

Group	Surgical cases		Medical cases		Difference between means*
	No	Mean improvement	No	Mean improvement	
		Males			
1	3	0 67 grade	0	—	—
2	4	2-00	2	0 50	1 50
3 A	5	1 80	2	0 50	1 30
3 B	2	2 00	3	0 67	1 33
4	2	1 50	1	1·00	0 50
5 A	3	1 33	0	—	—
5 B	1	2 00	1	—1 00	3 00
		Females			
1 A	3	1 33	4	0 50	0 83
1 B	1	1 00	3	0 33	0 67
1 C	3	2·00	3	0·00	2 00
2 A	1	2 00	1	1 00	1·00
2 B	3	1 00	4	0 25	0 75
2 C	5	1 20	2	0 50	0 70
3 A	3	0 67	5	0 20	0 47
3 B	2	2·00	6	0 33	1 67
4	1	0·00	2	1 00	—1 00
5 A	4	1 50	1	0 00	1 50
5 B	1	1 00	0	—	—
Total	47	1 43	42	0 38	1 05

* A positive value in the last column indicates that the surgical response was more favourable than the medical The relief of symptoms one year after treatment in the surgical group is on the average superior to the medical

TABLE II

COMPOSITION OF THE MATCHED GROUPS ON WHICH THE STATISTICAL ANALYSIS IS BASED THE THIRD CLASS COMPARISONS ARE DISCARDED

Group	No of surgical cases	No of medical cases for comparison		
		1st class	2nd class	3rd class
Males				
1	3	3	—	—
2	5	1	2	—
3 A	6	1	1	—
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1 B	1	3	3	4
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It must be emphasized strongly that the reliability of this analysis depends entirely on the validity of the grouping and matching of the cases described above In a clinical trial it is necessary that the allocation of cases to experimental and control groups shall be free from bias in respect of severity of symptoms, age, sex, or any other circumstance likely to have a bearing on prognosis This is usually contrived by a deliberately planned experi ment in which the cases are allotted to one or other form of treatment by a designed process In the present investigation, however, this was not done, each patient was given surgical or medical treatment as seemed appropriate without strict regard to the possible future use of the cases in a statistical comparison

It has been possible, however, owing to such factors as changing standards as to indications for operation, patients declining operation, and so on, to match our surgical groups with medical, on the basis of the observations made during the patient's first stay in hospital and thus the series of cases has been converted retrospectively into a properly con trolled experiment to the best of our ability All the patients had been under detailed observation in the wards of the hospital and had submitted to the same routine

In the statistical analysis each group was taken separately and the "surgical" cases compared with the 1st and 2nd class 'medical' cases therein Six criteria are available for statistical evaluation, these can be divided into two sections In the first these can be divided into two sections In the first these the observations made at periodic re-examinations of those patients who survived are considered particularly in regard to the following factors (1) retinal grade, (2) cardiac efficiency (3) renal

efficiency, (4) symptom grade, and (5) diastolic blood pressure   The second part is a consideration of the incidence of deaths in relation to sex, severity of symptoms and method of treatment.

COMPARISON BY SYMPTOMS AND SIGNS

In the analysis under this heading, the change was noted, for each patient, between the initial value or grade and that found at a specified time after treatment, in each of the items noted above   The choice of the time interval is of some importance   It is desirable to use as long a period as possible, to give ample time for the results of treatment to become manifest, a long interval also helps to reduce bias, by eliminating from the analysis all patients who die soon after the initial examination, and who therefore may have been too advanced in the disease to benefit from treatment   It also serves to minimize any effects attributable to psychological betterment and unintentional suggestion   On the other hand, increasing the time interval involves omission from the comparison of all the more recent cases The best compromise is to base the main comparison on the difference between the initial findings and those at the examination most nearly coinciding with the first anniversary of the commencement of treatment, or of sympathectomy

Data on change of symptom-grade are available for 47 surgical cases (20 male and 27 female) and 42 medical cases (11 male and 31 female), a total of 89 patients   Observations on criteria 1, 2, 3, and 5 (see p 288) are also on record for most of these cases   Comparisons of changes after three years were also made, but the number of cases was only 41, the findings for the one-year and three-year periods are fully concordant

Criteria 2, 3, and 4 are on the ABC scale, an arbitrary value of unity being given to each successive step   Retinal grade is 0, 1, 2, 3, and 4, as described earlier, blood pressure differences were measured quantitatively in mm Hg   In each group of patients the average change in the medically and surgically treated cases was calculated with respect to each criterion, and the probability that the observed difference, if any, might be attributable to chance fluctuations   The combined probability that all the differences with respect to treatment might be chance effects were then calculated   Where this probability is less than 1   20 the treatments are taken as giving significantly different results

Results of analysis   The main findings are as follows

(1) In the *symptom grading*, the surgical cases show a great and decisive superiority over the medical   The details for a 12-months interval are shown in Table III   A positive value in the last

TABLE III

MEAN CHANGES IN SYMPTOM GRADE AFTER ONE YEAR

Group	Surgical cases		Medical cases		Difference between means*
	No	Mean improvement	No	Mean improvement	
		Males			
1	3	0 67 grade	0	—	—
2	4	2·00	2	0 50	1 50
3 A	5	1 80	2	0 50	1 30
3 B	2	2·00	3	0 67	1 33
4	2	1 50	1	1·00	0 50
5 A	3	1 33	0	—	—
5 B	1	2·00	1	−1·00	3·00
		Females			
1 A	3	1 33	4	0 50	0 83
1 B	1	1·00	3	0 33	0 67
1 C	3	2·00	3	0·00	2·00
2 A	1	2·00	1	1·00	1·00
2 B	3	1 00	4	0 25	0 75
2 C	5	1 20	2	0·50	0 70
3 A	3	0 67	5	0·20	0 47
3 B	2	2·00	6	0 33	1 67
4	1	0·00	2	1·00	−1·00
5 A	4	1 50	1	0·00	1 50
5 B	1	1·00	0	—	—
Total	47	1 43	42	0 38	1·05

* A positive value in the last column indicates that the surgical response was more favourable than the medical The relief of symptoms one year after treatment in the surgical group is on the average superior to the medical

column means that the surgical cases did better
It will be seen that only in one group (female group 4,
with one surgical and two medical cases) is there a
minus sign   As might be expected, the combined
test of significance shows an infinitesimal probability
(less than 1   1,000,000,000) that the superiority of
the surgical cases is due to sampling fluctuation

On the average, the surgical cases improved by
about 1 4 symptom grades in the course of a year,
almost all were able to work, and many were free
from symptoms   In the medical cases, the average
improvement was less than 0 4 of a symptom grade

(2) In *diastolic blood pressure*, the medical cases
show an average rise while the surgical cases
show an average fall, and the difference is highly
significant statistically   The amount of rise or fall
did not seem to vary with the severity of the cases
It was therefore legitimate to pool all the surgical
and all the medical cases   The means and some tests
of significance are shown in Table IV   Although

TABLE IV

MEAN CHANGES IN DIASTOLIC BLOOD PRESSURE
AFTER ONE YEAR

Cases	No	Mean change (mm Hg)
Surgical cases	31	−8 39
Medical cases	30	+8 37
Difference		16 76±5 08
t		3 30
p		0 001 approx

the changes are statistically established, they are not
very striking in magnitude, averaging +8 4 mm Hg
in the medical cases and −8 4 mm Hg in the
surgical

(3) In the *retinal grading* there was a difference in
favour of the surgical cases, which is just statistically
significant   On the average the surgical cases
improved in twelve months by 0 5 of a grade, while
the medical cases showed no change

(4) & (5) *Cardiac* and *renal gradings* showed a
difference in favour of surgical treatment which,
however, in *neither case was statistically significant*

The general conclusion from this part of the
analysis is that among patients who survive a year
or more, those who received surgical treatment are
functionally and subjectively considerably better
than those treated medically   The surgical cases
also appear to be better on objective signs blood
pressure, and cardiac, retinal and renal gradings
But the difference in the well being of the patients
is much greater than would be expected from these
objective assessments

COMPARISON BY MORTALITY

We now come to the consideration of the second
part of the statistical analysis—the analysis of death
incidence   Including all surgical cases and the first
and second class medical comparisons, we have
records of 128 patients of whom 36 died   It was
soon obvious that the death rate in the benign cases
(groups 1 to 4 inclusive) was so widely different from
that in the malignant cases (groups 5A, 5B and 5C)
that those two classes were best treated separately

In the *benign* groups there are 45 surgical cases
with 5 deaths, compared with 55 medical cases
with 7 deaths   On the crude figures there is no
evidence of any difference   This is confirmed by
more refined analysis   These patients were of
disparate ages   and had been under observation for
periods varying from a few months to several years
The older the patient, and the longer the period
under observation   the greater the risk of death
For each patient was calculated the chance of dying
during the period of observation if he or she had the
same death risk as prevailed for persons of like
age and sex in the general population   as listed in the
Life Table for Scotland for 1931   The period of
risk for survivors was taken as the time since the
first examination   and for deceased patients as the
period from the first examination until death   The
sum of the figures for all the patients in a group
gives the number of ' expected deaths '   The data
are shown in Table V

It will be seen that there were 5 deaths in surgical
cases, against the expectation of about 1 1 and 7
in medical cases against the expectation of about
1 3 deaths   This indicates that the death rates for
persons with benign essential hypertension seeking
hospital advice is about 5 times that prevailing in the
population as a whole, and there is no evidence on
these small numbers, of any difference between
medical and surgical cases

THE MORTALITY RATE IN MALIGNANT
HYPERTENSION

Of the original medical group of 20 malignant
hypertensive patients 2 were unsuitable for in
clusion in the statistical analysis   one being a third
class comparison already discarded and the other
dying a few days after admission to hospital   There
remains for consideration the 10 surgical patients
of whom 5 died and 18 medical patients of whom
17 died   At first sight this suggests a strong recom
mendation of surgical treatment but further detail
is necessary to ensure that the groups are comparable
All the cases surgically treated were regarded as
suitable for operation by both physicians and
surgeons with the exception of one patient a woman
who had been in congestive heart failure prior to

TABLE V

DEATHS IN PATIENTS WITH BENIGN HYPERTENSION*

Group	Surgical cases			Medical cases		
	No of patients	Deaths		No of patients	Deaths	
		Expected	Observed		Expected	Observed
			Males			
1	3	0·07	1	3	0 06	0
2	5	0 29	0	3	0 08	2
3 A	6	0 19	0	2	0·04	0
3 B	2	0·02	0	3	0 09	0
4	2	0 04	0	2	0 03	1
All male	18	0 61	1	13	0 31	3
			Females			
1 A	3	0 04	0	4	0 07	0
1 B	1	0·01	0	6	0 23	0
1 C	3	0·09	0	5	0 16	1
2 A	2	0 02	0	2	0 05	0
2 B	4	0·08	1	4	0 07	0
2 C	7	0 16	2	5	0 12	0
3 A	3	0 06	1	5	0 08	1
3 B	3	0·05	0	7	0 23	0
4	1	0 02	0	4	0·04	2
All female	27	0 51	4	42	1 02	4
Total	45	1 12	5	55	1 33	7

* By comparing the expected deaths with the observed, the death rate in benign hypertension is approximately five times that prevailing in the population as a whole   There is no significant difference between our two groups of medically and surgically treated patients

admission to hospital   In this case the surgeons were reluctant but were finally persuaded to intervene

The medically treated cases were graded in three categories   (A) where there was no contraindication to surgical treatment, (B) where the physicians thought operation justifiable although one criterion fell short of the desirable level, and (C) cases where neither physicians nor surgeons would advise operation, that is with severe renal or cardiac failure or both combined

The surgical cases described above fell into category (A) with the exception of the one stated, who was graded (B)   Details of the cases in these surgical and medical categories are given in Table VI

It will be seen that of the 9 surgical (A) cases, 5 died after an average period of 13 months and 4 have lived for an average of 26 months after being first treated   There are 5 medical (A) cases all of whom died after an average interval of 5 months   The only surgical (B) case has not died after an interval of 14 months, out of 9 medical (B) cases, 8 died after an average of 1 8 months, and one has survived for the short period of 3 5 months   The 4 medical (C) cases died after an average interval of 1 3 months

The only valid control for the main body of surgical malignant cases is the (A) group of medical patients   As far as they go the comparative death rates in (A) and (B) categories appear to favour surgical treatment   The data however are insufficient for a definite decision   The physicians in charge of the medical (A) cases are of the opinion, on clinical grounds, that these patients would have lived longer had they been treated surgically, but for statistical purposes a much larger series of malignant cases is required   It seems unlikely that this will be obtained in cases fit enough for operation, because this will not be refused in future merely in order to provide a control group   But there is a prospect of an entirely ethical future experiment   In the (B) cases, where the physicians believe operation would be beneficial and the surgeons regard it as too hazardous, the opinion of the surgeons has hitherto usually prevailed   If it could be agreed that in future half these cases, chosen by a random process, could be operated on, and the other half kept as controls, decisive information about the value of operation in the most severe cases might be forthcoming   Since in the absence of surgical treatment these patients have an

KEITH, WOOLF, AND GILCHRIST

TABLE VI

DEATHS IN PATIENTS WITH MALIGNANT HYPERTENSION

(A) No contraindication to surgical treatment

		Died				Survived		
	Group	Sex	Age	Months lived	Group	Sex	Age	Months observed
Surgical (9 cases)	5 A	M	46	9	5 A	M	44	18
	5 B	M	61	10	5 A	M	47	50
	5 C	M	45	5	5 A	F	45	22
	5 A	F	36	13 5	5 A	F	45	14
	5 A	F	45	29				
	5 cases			Mean 13 3	4 cases			Mean 26 0
Medical (5 cases)	5 A	M	40	1				
	5 A	M	44	2				
	5 B	M	60	6				
	5 A	F	57	12				
	5 A	F	31	5				
	5 cases			Mean 5 2				

(B) One criterion against surgical treatment

		Died				Survived		
	Group	Sex	Age	Months lived	Group	Sex	Age	Months observed
Surgical (1 case)					5 B	F	44	14
Medical (9 cases)	5 A	M	49	5	5 C	M	56	3 5
	5 A	M	50	2				
	5 A	M	66	0 5				
	5 A	M	54	1				
	5 B	M	53	1				
	5 C	M	64	3				
	5 A	F	48	1				
	5 B	F	49	1				
	8 cases			Mean 1 8	1 case			3 5

(C) Severe cardiac or renal failure

	Group	Sex	Age	Months lived	
No surgical cases					
Medical (4 cases)	5 A	M	51	0 3	
	5 C	M	53	0 5	
	5 C	M	48	3	
	5 B	F	56	1 5	
	4 cases			Mean 1 3	

average expectation of life of less than two months, no harm can be done by operation, and possibly some good to the patients, as well as providing an advance in knowledge

In malignant hypertension surgical treatment seems to lead to greater well-being in surviving patients on a larger scale than would be deduced from the concomitant small remission of objective findings There are indications, falling short however of statistical significance that the risk of death may be lowered by operation Valuable evidence could probably be obtained if operation were performed on alternate cases for which physicians recommend operation and surgeons disagree

SUMMARY AND CONCLUSIONS

One hundred and fifty-one patients, suffering from essential hypertension, form the basis of the present study. They have been carefully investigated and their progress observed over a number of years.

For comparative purposes they have been divided into two groups. The first, numbering 96 patients, received purely medical treatment—rest and sedation. The second group, composed of 55 patients, was submitted to sympathectomy.

Largely as a result of changing standards regarding the indications for surgical intervention and with widening experience of the procedure over the past nine years, it has been possible retrospectively to match our surgical group in their pre-operative state with a corresponding series of medical cases in whom for one reason or another surgery was not employed.

By subdividing the medical and surgical cases into smaller categories alike in sex, age, retinal state, cardiac and renal function, and diastolic blood pressure, as determined before the start of therapy, accurate comparison was facilitated and the findings observed a year later in each group reassessed. The results thus obtained have been submitted to statistical analysis. For a variety of reasons 22 medical cases were found unsuitable for comparison and were discarded.

The statistical investigation indicates that in benign hypertension at the end of one year and also at the third anniversary of surgical treatment the sympathectomized patients experience a greater relief of symptoms than corresponding medical groups. Almost all in the surgical group were able to work and many were free from symptoms.

By the end of a year the diastolic blood pressure showed on the average a fall of approximately 8 mm Hg in the surgical group, whereas amongst those patients treated exclusively by medical measures it had tended to rise by about an average of 8 mm after the same length of time. In the surgical group there was also a slight improvement in the retinal grade. In this respect the medical cases showed no change.

The general conclusion is that when our two groups are compared those patients who receive surgical treatment for their benign hypertension are subjectively considerably better than those treated medically. There is less change in the level of the diastolic pressure.

The death rate for persons whose symptoms of so-called benign hypertension lead them to seek help in the hospital is about five times that prevailing in the population as a whole. From our small numbers submitted to analysis there is no evidence of any difference in the mortality rates in the two groups of medically and surgically treated patients.

In malignant hypertension, the data available from a comparatively small number of patients—30 in all—suggest that surgery leads to greater well-being in survivors, but a much larger series is required if statistical proof is to be obtained.

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SOCIÉTÉ EUROPEENNE DE CARDIOLOGIE

The following communication from the Societe Europeenne de Cardiologie (European Cardiological Society) is printed for the information of the members of the British Cardiac Society It has not yet been considered by the British Cardiac Society or by its Council and its publication is for information and must not be taken as meaning that the details have been accepted

Le 29 janvier 1949 se sont reunis à Buxelles des cardiologues, représentant quatorze nations européennes, dans le but de constituer la Societe Europeenne de Cardiologie

Les statuts provisoires suivants ont éte adoptes

(1) La Société Européenne de Cardiologie se propose do grouper les cardiologues de toutes les nations d'Europe

(2) La Societé Europeenne de Cardiologie a pour but de contribuer au développement de la cardiologie, de favoriser la collaboration scientifique, d'aider aux rapprochements personnels Dans le domaine de la pratique cardiolôgique la Societé Européenne de Cardiologie peut être amenee à donner des directives d'ordre moral

(3) La direction de la Société sera assuree par

(a) Un Bureau compose d un President d hon neur, d un Président, de trois Vice-Présidents, d un Secrétaire general et d'un Tresorier

(b) Un Comite constitutif compose des delegues officiels reunis a Bruxelles à l assemblée constitutive Ce Comité pourra être elargi ultérieurement

(4) Une reunion du Bureau et du Comité con stitutif aura lieu au moins tous les deux ans Toutefois, le President a pouvoir de prendre toute decision d urgence pourvu qu il ait recueilli l appro bation ecrite de la majorite des membres du Comité constitutif

(5) La Societe comprendra des membres titulaires, correspondants et honoraires

(6) Tout cardiologue européen peut faire partie de la Societe pour autant que sa candidature ait ete parrainée par la Societe a laquelle il appartient, u son defaut par son délegue national, a son defaut par un membre du Comité constitutif

(7) Pour entretenir les rapports entre les membres et etendre l action de la Societé Européenne de Cardiologie, le Comité organisera, en principe tous les deux ans, un Congrès Il s intercallera entre les réunions de l'Association Pan Americaine de Cardiologie

(8) Le Bureau et le Comite constitutif ont l'autorisation de chercher les appuis financiers nécessaires pour subvenir aux activités courantes, pour organiser des reunions scientifiques, etc

(9) Le nouveau groupement devra, en temps voulu, avec la Societé Pan Américaine de Car diologie, former la Societe Internationale de Cardiologie

(10) Toute question non envisagee dans ces statuts sera traitee dans le reglement d ordre interieur

Bruxelles le 29 janvier 1949

EUROPAN CARDIOLOGICAL SOCIETY

On January 29, 1949, a meeting took place at Brussels between delegates of fourteen European countries in order to constitute a European Cardiological Society

The following provisional by-laws have been agreed

(1) The European Cardiological Society proposes to group the cardiologists of all the European nations

(2) The aims of the European Cardiological Society are to foster the development of cardiology, to further scientific exchanges and to help personal contacts of those working in this speciality The

European Cardiological Society may also be called upon to give moral directives in the sphere of prac tical cardiology

(3) The administration of the Society will be entrusted to

(a) A Council consisting of an Honorary Presi dent, a President, three Vice Presidents a General Secretary and a Treasurer,

(b) A Constitutive Committee consisting of the official delegates present at the constitutive Assembly in Brussels This Constitutive Committee may be enlarged at a later date

(4) A meeting of the Council and the Constitutive

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Committee will take place at least biennially In case of emergency, however, the President has authority to take the necessary decisions without a meeting, providing he has obtained the written agreement of the majority of the Constitutive Committee

(5) The Society will consist of active members, corresponding members, and honorary members

(6) Membership of the Society is open to all European cardiologists providing their admission is recommended by the Society to which they belong or by their national delegate or by a member of the Constitutive Committee

(7) It is suggested that, if possible, a biennial Congress will be organized in order to maintain close collaboration between the members and enlarge the Society's activities These Congresses will be held at intervals between those of the Pan-American Cardiological Association

(8) The Council and the Constitutive Committee of the Society have authority to seek financial assistance to cover the necessary expenditure inherent to current activities, the organization of scientific meetings, and any other purposes decided by Committee

(9) The new Society will, in due course, together with the Pan-American Cardiological Society, form the International Cardiological Society

(10) All matters not dealt with in the present *By-Laws* will be subject to Regulations

Brussels, January 29, 1949.

Great Britain
(s) D Evan Bedford

Belgium
(s) Pierre Rylant, François van Dooren

Denmark
(s) Kaj Larsen

Spain
(s) Antonio Crespo-Alvarez Trias de Bes

Finland
(s) Pentti Halonen

France
(s) Charles Laubry, Jean Lenegre

Greece
(s) Demosthene Papapanayotou

Holland
(s) Formijne

Italy
(s) Camillo Colombi

Norway
(s) Hakon Rasmussen

Portugal
(s) Eduardo Coelho

Sweden
(s) Gustav Nylin, Gunnar Biorck

Switzerland
(s) Ivan Mahaim

Jugoslavia
(s) Cedomil Plavsic

The *provisional Council of the European Cardiological Society* is constituted as follows

Honorary President
    Professor Charles Laubry (France)
President
    Professor Gustav Nylin (Sweden)
Vice-Presidents
    Doctor D Evan Bedford (Great Britain)
    Professor Jean Lenegre (France)
    Professor Eduardo Coehlo (Portugal)
General Secretary
    Doctor François van Dooren (Belgium)
Treasurer
    Doctor Ivan Mahaim (Switzerland)

ABSTRACTS OF CARDIOLOGY

Cholesterol and Myocardial Infarcts H LALIBERTÉ and M VACHON *Laval méd*, 13, 294–302, March, 1948

Cardiac infarction may occur in a young man or woman, in whom there is no evidence of syphilis or hypertension The authors discuss 39 such cases in patients varying in age from 28 to 47, 11 of whom were women and 28 men, and in which the ultimate cause of the infarct was thought to be fatty deposits in the small arteries due to a raised blood cholesterol In hereditary xanthomatosis there is a disturbance of the lipid metabolism, and, although fatty deposits in skin and mucous membrane are not always seen, abdominal angina and infarcts sometimes occur, there is always a raised blood-cholesterol in such cases In 7 cases of cardiac infarction, the only common factor was a high level of cholesterol in the blood In only 2 cases was necropsy possible in both there was an exten sive infarct of the left ventricle, the arteries being stuffed with yellow plaques with little sign of fibrosis All patients had a normal blood pressure, and most had had previous attacks of præcordial or abdominal pain The authors conclude that the sterols play an important, perhaps a primary, role in the causation of arterial occlusion *T E C Early*

Clinical Features in Coarctation of the Aorta A Review of 96 Cases N A CHRISTENSEN and E A HINES *Proc Mayo Clin*, 23, 339–342, July 21, 1948

At the Mayo Clinic between 1925 and 1947 coarctation of the aorta was diagnosed in 119 cases Males predomi- nated over females in the ratio 3 8 to 1 Only 26% of the patients were below 20 years of age—the period of life when surgery is best tolerated In 30% the condition was discovered incidentally high blood pressure frequently pointed to its presence, but only 3 patients gave a history of intermittent claudication Palpation of the larger arteries to detect differences in pulsation is more reliable than the smaller limb arteries Differences in arterial pulsation and pulse pressure in the arms may aid in locating the site of the coarctation In 80% there was evidence of collateral circulation over the scapular and interscapular regions and somewhat less frequently over the supraclavicular and internal mammary regions

Cardiovascular murmurs were present in 94% the most frequent being a fairly loud systolic bruit over the base of the heart Basal diastolic murmurs were heard in 20% and were probably associated with valvular lesions In 25% there was a ray evidence of cardiac enlargement and in 30% electrocardiographic evidence of left ventri cular preponderance Ophthalmoscopic examination showed general narrowing of the retinal arterioles, parti- cularly in the cases with hypertension but no patient had hypertensive retinopathy Renal function studies

revealed no abnormality and this possibly accounts for the absence of severe hypertensive disease Important features in establishing the diagnosis were found to be (1) characteristic differences in arterial pulsations and in direct and indirect blood pressure readings between the upper and lower limbs (2) evidence of well developed collateral circulation (3) rib notching in the presence of one or more cardiac or cardiovascular murmurs *H E Holling*

The Treatment of Angina Pectoris with Propylthiouracil G HOLLANDER and H MANDELBAUM *Ann intern Med*, 28, 1150–1156, June 1948

Ten patients with angina pectoris and hypertension were treated with propylthiouracil in the Jewish Hospital Brooklyn, N Y Initially a dose of from 50 to 100 mg was given daily this was increased to a maximum of 200 mg daily Improvement took place within 8 weeks in 4 of these patients and 2 of them were able to resume work Two became progressively worse during treat ment No correlation could be found between the levels of the basal metabolic rate and improvement in symp- toms One case with an initial figure of −8% became free from attacks when the level fell to −26%, 3 more cases, in which the initial levels were raised improved while the rate was still above normal limits The blood cholesterol levels often did not rise as the basal metabolic rate fell No toxic effects on the blood were observed but water retention occurred in 7 patients causing dyspnœa and œdema of the legs *C H C Bain*

Experiences with the Use of Heparin and Dicumarol in the Treatment of Coronary Thrombosis and Thrombo- embolic Disease J B VANDER VEER D S MARSHALL and P T KUO *Trans Stud Coll Phys Phila* 16 67–72, June, 1948

The authors, working in the Pennsylvania Hospital Philadelphia, have participated in a controlled study sponsored by the American Heart Association to deter mine the value of dicoumarol therapy in coronary occlusion with myocardial infarction There were 35 treated cases and 51 controls Prothrombin times were kept so far as was possible between 30 and 35 seconds control times being 13 to 15 seconds The initial dose of dicoumarol was 300 mg daily for 2 or 3 days the maintenance dose somewhat less than 100 mg daily treatment was continued for about a month Among the controls thrombo-embolic complications occurred in 12 patients 9 of whom died there were also 9 deaths from other causes In the treated cases thrombo- embolic complications occurred in 6 with a fatal ending in 2 there was 1 other death

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The results of a preliminary analysis of the first 800 cases of cardiac infarction treated with dicoumarol which were collected by a special committee of the American Heart Association are also given. The death rate in the controls was 23%, in dicoumarol-treated cases 13%. Thrombo-embolic complications occurred in 19% of the untreated and in 9% of the treated patients. Hæmorrhagic manifestations of one type or another were encountered in 4% of the controls and in 11% of the treated cases, but serious hæmorrhage was rare.

The value of anticoagulants in the treatment of simple phlebothrombosis or thrombophlebitis is again stressed. In 23 untreated cases there were 9 deaths; in 30 cases treated by venous ligation, 3 deaths; in 49 cases treated with heparin and dicoumarol there was only 1 death. It is admitted that selection of cases was weighted against the controls.   *Paul Wood*

Left Vocal Cord Paralysis Associated with Cardiac Disease. D A DoLOWITZ and C S LEWIS. *Amer J Med* 4 856–862, June, 1948

The literature on the mechanism of paralysis of the left recurrent laryngeal nerve in cases with cardiac enlargement is reviewed, and 2 personal cases are described. One patient had mitral and aortic valvular disease with marked enlargement of the left auricle, the other had atrial septal defect, possibly with mitral stenosis (Lutembacher's syndrome) and greatly enlarged pulmonary conus. The area bounded by the aortic arch superiorly, the pulmonary artery inferiorly, and the ligamentum arteriosum medially was carefully examined in 5 fresh and 22 fixed cadavers, and a group of three to four lateral tracheo-bronchial lymph nodes was constantly found in close proximity to the left recurrent nerve. It is pointed out that these lymph nodes may effectively compress the nerve when accompanied by cardiac hypertrophy, engorgement of the pulmonary artery, or both. *A Schott*

Comparison of the Fick and Dye Injection Methods of Measuring the Cardiac Output in Man. W F HAMILTON, R L. RILEY, A M ATTYAH A COURNAND D M FOWELL, A HIMMELSTEIN, R. P NOBLE, J W REMINGTON D W RICHARDS, N C WHEELER, and A C WITHAM. *Amer J Physiol* 153, 309–321, May, 1948. 2 figs, 17 refs

Cardiac output can be determined from the time-concentration curve in arterial blood (obtained from rapid serial samples) of a dye injected rapidly into a vein. This and the direct Fick method (cardiac catheterization) were compared in 48 almost simultaneous determinations in 31 subjects including normal subjects at rest and during light and heavy exercise and patients suffering from various cardio-respiratory disease at rest and during occasional light exercise. The technique of determining cardiac output by the dye injection method is described in detail. The results agreed within 25% in all but 6 determinations. The distribution of results about the line of identity was symmetrical, so that the averages for each method were almost identical. The dye method, owing to its rapid performance and its nature is more apt

to reflect physiological variations. The sources of error in it are discussed, the chief being recirculation of blood (containing dye) during the determination.
                                    R A Gregory

The Phenomenon of Skin Hyperalgesia in Angina Pectoris. E V LEVINSON. *Klin Med Mosk*, 26, No 9, 47–55, 1948

In 145 patients with anginal pain areas of cutaneous hyperalgesia were repeatedly mapped out with a view to evaluating their diagnostic significance and their relation to the results of treatment. Cutaneous hyperalgesia was most commonly present in the C2 to C4 and D1 to D5 dermatomes, rarely in the C5 to C7 and D6 dermatomes. These zones were not static in any one patient but were liable to change if the irradiation of the pain changed. They were always present in patients whose attacks were frequent or prolonged, but were only found in 79 % of the whole series. When patients were tested within 3 days of an attack, areas of hyperalgesia were present in 93%. Their disappearance is considered to be a valuable index to the success of treatment. *S S B Gilder*

Studies on the Blood Flow in the Extremities in Cases of Coarctation of the Aorta. Determinations Before and After Excision of the Coarctate Region. K G WAKIM, O SLAUGHTER, and O T CLAGETT. *Proc Mayo Clin*, 23, 347–351, July 21, 1948

Plethysmographic measurements of the blood flow to the arm and leg in 14 normal persons at rest and 14 patients with aortic coarctation revealed no significant difference between the two groups, and in 9 cases no change in blood flow followed surgical removal of the coarctation. *H E Holling*

The Relationship of Retinal Hemorrhages in Hypertensive Patients to Cerebral Hemorrhage. A Comparison of the Retinal Picture in Hypertensive Individuals who Died of Heart Failure with those who Suffered a Cerebral Hemorrhage. L A. SOLOFF and C T BELLO. *Amer J med Sci*, 215 660–664, June, 1948

Cerebral hæmorrhage is the cause of death in nearly one-third of hypertensive individuals. The final mechanism of the hæmorrhage is ill understood. It has been ascribed to the development of miliary aneurysms, to ischæmia of brain tissue and weakening of support for the blood vessels, to disease and rupture of the walls of veins and, more recently, to capillary weakness. The latter factor has been associated with the occurrence of retinal hæmorrhage.

On a re-investigation, retinal hæmorrhages were found to have been present in 5 out of 17 patients who had had a cerebral hæmorrhage. Retinal hæmorrhage was present in 14 out of 18 patients with hypertension who died of cardiac failure without cerebral hæmorrhage. Retinal hæmorrhages occurred more frequently in patients with large areas of 'spasm' of the retinal arteries than in subjects with marked thickening of these vessels. It is

concluded that retinal hæmorrhages cannot be used as a prognostic sign of future cerebral hæmorrhage

J McMichael

True Aneurysms of the Mitral Valve in Subacute Bacterial Endocarditis. O SAPHIR and E P LEROY *Amer J Path*, 24 83–95, Jan, 1948

Mycotic aneurysms of the mitral valve were found in 5 out of 12 cases of subacute bacterial endocarditis treated with sulphonamide preparations, heparin or penicillin These cases were observed between 1943 and 1946 the authors were unable to find an example of mycotic aneurysm formation in 41 cases of subacute bacterial endocarditis seen between 1935 and 1943 Rupture of the aneurysm occurred in 4 cases, and the increased incompetence of the mitral valve may have contributed to death The aneurysms probably arise in areas of granulation tissue situated in the substance of the valve The authors suggest that the aneurysms represent attempts at healing of the endocarditis, perhaps as a result of the increasing use of chemotherapeutic agents in recent years   *R H D Short*

The Action of Neostigmine in Supraventricular Tachycardias S WALDMAN and L PELNER *Ann intern Med*, 29, 53–63, July, 1948

The action of neostigmine methylsulphate (or ' prostigmin) on sinus tachycardia and auricular and nodal paroxysmal tachycardias is discussed, the paper includes case notes and electrocardiograms of 5 patients The tracings demonstrate the slowing of sinus tachycardias with rates of about 130 per minute to about 80 per minute *within about 20 minutes of the injection of 1 mg of neostigmine*, and the restoration of normal rhythm in a case of auricular tachycardia and in one of nodal tachycardia 5 minutes after injection Immediately on the return of sinus rhythm the P–R interval is prolonged but becomes normal within a few minutes In another case of auricular tachycardia the abnormal rhythm persisted after the injection, but there was an immediate and progressive effect on A-V conduction so that 33 minutes after the injection there was 3 1 4 1 A-V block Two days later normal rhythm was recorded

The influence of neostigmine on these types of tachycardia is believed to be due to *its action on the myoneural junctions of parasympathetic vagus fibres in the* S A and A-V nodes and in auricular muscle The drug augments vagus activity at these sites by inhibiting the action of cholinesterase If these tachycardias result from the action of sympathomimetic amines on the heart, the use of the parasympathomimetic drug neostigmine is rational therapy   *S H Cookson*

Continued Hypertension Prognosis for Surgically Treated Patients R. H SMITHWICK *Brit med J* 2, 237–243, July 31, 1948

It is necessary to turn to the U.S A for any large series of patients treated surgically for hypertension the author describes his second series in this paper The

operations were performed in Boston Massachusetts, and the author s own lumbo-sacral technique was employed All of the 256 patients were suffering from continuous essential or malignant hypertension and had been operated upon at least 5 and at the most 9½ years previously

The state of the cardiovascular system was evaluated before and after operation with particular reference to the cerebral, retinal cardiac and renal areas Intravenous pyelography was carried out as a routine, and the blood pressure data were so far as possible obtained in a standard fashion Male patients comprised 39 4%, and females 60 6% of the series The total mortality during the 5 to 9 year period of observation was 31%, the mortality among males being 34% and among females 29% The causes of death were cerebral, cardiac renal and miscellaneous, in that order with a heavy preponderance in the very young and the older age groups The prognosis became poorer as the degree of eyeground abnormality increased and the same applied to the cardiovascular findings The presence of arteriosclerosis was associated with a particularly poor prognosis It had been previously noted that in a follow up period of 1 year to 5 years the blood pressure levels were lowered significantly in the majority of unselected patients but in the period of 5 to 9 years this lowering is not maintained and there has been a return of the pressure to pre operative levels in 44% of cases There was evidence, however, of the slowing up of the rate of progress of cardiovascular disease, and this may prove to be a very important accomplishment Comparison with medical treatment is made as much as possible but the major handicap is the absence of reliable and adequate medical statistics Such comparisons as can be made at this time *while admittedly inadequate, suggest that surgical treatment has favourably altered the prognosis in many cases of continued hypertension and cardiovascular disease*

H T Simmons

Asynchronous Activity of the Dog's Heart After Section of the Right Branch of the Bundle of His A I SMIRNOV *Arkh Patol* 10 No 3, 7–13 May–June 1948

The influence of section of the right branch of the bundle of His on the action of the heart was observed over a period of 6 years in a dog During the first days after the operation a reduplicated first heart sound became audible at the apex Three weeks later a systolic murmur became audible over the whole thorax This murmur disappeared just before the death of the dog

Six weeks after the operation atypical Wenckebach's were present in leads II and III indicating that the right bundle of His had been severed Repeated X ray examination showed a gradual dilatation of the right ventricle Changes in the electrocardiogram developed slowly after the operation During the last days before the dog died of heart failure a marked œdema and ascites developed Post mortem examination showed that the right branch of the bundle of His had been correctly cut and that its ends had not united again Hypertrophy and degeneration of the right myocardium and a relative tricuspid incompetence were found The

compensation of the right ventricle (hypertrophy and dilatation) had succeeded in maintaining normal circulation over a period of 4 years. This compensation, however, failed after 6 years causing death of the animal. No synchronous rhythm with the left ventricle occurred during the 6 years after the operation

J Flaks

Serum Protein in Cardiac Patients G Biorck, S Hedlund, J Karnell, and H Karni *Nord Med*, 38, 1179–1182, June 11, 1948

The authors report the results of serum protein estimations on 147 hospital patients with various forms of heart disease. Globulin is rarely reduced but albumin is in two-thirds of the cases especially if there is heart failure, œdema, or evidence of liver disease as shown by the other usual tests. Owing, however, to the multiplicity of factors governing the concentration of protein in the blood (absorption, utilization, synthesis, dilution and loss) and the fact that most of these factors are affected in some way by cardiac decompensation, interpretation is very difficult

In recovery from heart failure the albumin content increases as does also the erythrocyte sedimentation rate possibly due to a rapid increase in fibrinogen. These increases are thought to be due to improvement in liver function and appear to be little related to diet, though the authors recommend use of protein hydrolysates. They admit however that no increase in the serum proteins may be detectable while decompensation persists and stress the importance of not giving hydrolysates, which contain an appreciable amount of salt'

A M M Wilson

Serum Cholesterol Values in Cardiac Patients G Biorck and H Karni *Nord Med* 38 1175–1179 June 11 1948

The authors discuss the value of cholesterol estimations in patients with heart disease based on the estimations carried out on 314 patients in the cardiac clinic of the Södersjukhus in Stockholm. Sackett's modification of Bloor's method was used

The values varied considerably within an age group or disease group and even in the same patient at different times but on the whole values were higher in women than in men in old people than in young ones, and in patients with cardiac sclerosis than in those with other types of heart disease. The level tended to fall after admission to the ward irrespective of the diagnosis. The authors conclude, in agreement with Josephson (*Nord Med* 1947 33 498), that a single estimation is almost useless and that though repeated ones may be of diagnostic assistance in cases of liver disease essential hypercholesterolæmia and thyroid disease they are of very doubtful value in the differential diagnosis of cardiovascular conditions

A M M Wilson

Carotid Artery Thrombosis. Report of Eight Cases due to Trauma H W Caldwell and F C Hadden *Ann intern Med* 28 1132–1142, June 1948

The authors describe 8 cases of carotid artery throm-

bosis seen in a military hospital in 1945. The thrombosis was due to trauma of the common carotid following penetrating wounds of the neck. Patients were usually comatose on admission to hospital with changes in the pupil reactions on the affected side and signs of hemiplegia on the other. Absence of pulsation over the temporal artery from involvement of the external carotid was found to be a valuable confirmatory sign. One patient recovered after heparin was administered the remainder died. There were 5 necropsies in 1 case the thrombus had extended as far as the circle of Willis in 2 cases major cerebral vessels were blocked by emboli. The authors consider that this condition may be more common in war surgery than has been supposed

C W C Bain

Chronic Infection and Atherosclerosis. Some Additional Experimental Data N W Jones and A L Rogers *Arch Path* 45, 271–277, March 1948

There is some clinical and experimental evidence that chronic infections, especially of the gall-bladder and paranasal sinuses, may play a part in the causation of atherosclerosis and associated heart failure. Micro-organisms were found in sections of the thickened thrombosed small arteries of chronically hyperplastic sinus tissues removed at operation. Similar organisms were sometimes demonstrated in sections of thrombosed coronary arteries from patients dying of acute coronary thrombosis. Micro-organisms introduced into the paranasal sinuses or paralaryngeal lymph nodes of cats could be demonstrated in the walls of the aorta and coronary arteries. Trypan-blue granules introduced into the paralaryngeal lymph nodes were demonstrated in phagocytic cells within the walls of the aorta and coronary arteries

Martin Hynes

Effect of Choline in the Prevention of Experimental Aortic Atherosclerosis A Steiner *Arch Path* 45 327–332 March, 1948

Rabbits were given 1 g of cholesterol with their food three times weekly. A well-controlled experiment showed that the addition to the diet of 0.5 or 1 g of choline hydrochloride daily delayed the development of atherosclerosis for 80 days or more. The effect was greater with the larger dose of choline. Hypercholesterolæmia was equal in the control animals and in those receiving choline

Martin Hynes

Vitamin E in Heart Disease. H Levy and E P Boas *Ann intern Med*, 28 1117–1124 June, 1948

Vitamin E (α-tocopherol) was given without benefit to 13 patients suffering from heart disease with relatively fixed symptoms. The series comprised cases of angina pectoris and cardiac failure due to coronary disease or rheumatic valvular disease. The drug was given in doses varying between 200 and 800 mg daily and administration was continued for from 7 to 12 weeks. In one case of angina pectoris there was a temporary improvement for the first two weeks, but the attacks then

continued at their former frequency In no other case was the number of anginal attacks affected, nor did any of the signs abate in those with cardiac failure The authors conclude that the use of vitamin E in heart disease is not warranted *C W C Bain*

The Effect of Dicumarol on the Heart in Experimental Acute Coronary Occlusion H L BLUMGART, A S FREEDBERG, P M ZOLL, H D LEWIS, and S WESSLER *Amer Heart J*, 36, 13–27, July, 1948

The administration of dicoumarol does not retard the healing process or the development of collateral circulation in dogs with experimentally produced myocardial infarction *R T Grant*

Coronary Deaths in " Healthy " Young Soldiers A Clinicopathologic Study N E REICH *Amer Practit*, Phila, 2, 731–747, July, 1948

Coronary artery disease as a cause of death in young subjects received little attention until the war of 1939–45 The present article deals with findings in 11 " healthy " soldiers ranging in age from 22 to 38 years who died from coronary artery disease These men had been subjected to frequent medical examination, but the results were negative In 7 over-weight was thought to be a predisposing factor, the effects of alcohol and tobacco were considered to be negligible The symptoms were generally atypical in those patients surviving more than an hour Pain was present in the epigastrium, left chest, or præcordium Usually it did not radiate although in one case there was continuous pain in the jaw for 3 days and in another left shoulder pain Contrary to accepted ideas, the onset of pain was always in the waking hours and pain was not associated with any strenuous activity Six of the patients died within an hour, and 5 lived for from 2 to 33 days At necropsy half of the cases showed significant cardiac hypertrophy Severe coronary sclerosis was present in 6 of 8 cases with actual thrombosis, and was moderate in 2 others Two patients had sclerosis without thrombosis and in one there was a coronary embolism with arteritis and septic thrombosis of the smaller coronary branches *James W Brown*

Excessive Hypertension of Long Duration A M BURGESS *New Engl J Med* 239, 75–79, July 15 1948

From patients seen in private consultation since 1914, 100 consecutive patients were selected in whom hypertension (systolic pressure greater than 180 or diastolic pressure greater than 100) had existed for more than 8 years Of the 100 patients 32 were between 28 and 50 years of age, 39 between 51 and 60, and the remaining 29 between 61 and 77 The shortest duration of hypertension was 9 years, the longest 25 years In 1947 53 patients were dead, 30 were in good health 17 were incapacitated to a greater or lesser degree The effects of sex, age, height of systolic and diastolic pressures had little effect on the actual duration of life

This study emphasizes the good prognosis in uncomplicated, benign or non progressive hypertension *W T Cooke*

Preoperative and Postoperative Studies of Intraradial and Intrafemoral Pressures in Patients with Coarctation of the Aorta G E BROWN, O T CLAGETT H B BURCHELL, and E H WOOD *Proc Mayo Clin* 23 352–358 July 21, 1948

Intraradial and intrafemoral pulse waves were recorded by means of a hypodermic strain gauge manometer in a series of patients with coarctation of the aorta The characteristic findings were an increase in the systolic and diastolic pressures in the radial arteries and a reduced systolic, though often with an increased diastolic pressure in the femoral artery The onset of the femoral pulse wave is often delayed When the stenosed portion of the aorta was resected and an end to-end anastomosis carried out the findings reverted to normal, but when the stenosed portion was excised and the subclavian artery anastomosed with the distal aorta the delay in the femoral pulse wave disappeared though the femoral pulse pressure was still reduced The findings could not be correlated with the clinical response of the patient to the procedure *H E Holling*

The Surgical Treatment of Coarctation of the Aorta O T CLAGETT *Proc Mayo Clin* 23 359–360 July 21

Between 10 and 20 years of age is regarded as the most suitable age for operation in cases of coarctation of the aorta Before the age of 10 the aorta is not large enough for satisfactory anastomosis and it is not known whether the ring of scar tissue left in the aorta at the site of the anastomosis will increase in size as normal growth and development take place Above the age of 20 considerable vascular damage may have occurred and good results cannot be expected At operation it is found that the length of the stenosed portion varies considerably in cases in which the two divided ends of the aorta could not be brought together the author has anastomosed the subclavian artery to the caudal end of the divided aorta The results of this procedure however have not been so good as was hoped *H E Holling*

The Blind Spot in Hypertension B G TOVBIN *Klin Med Mosk*, 26 No 9 39–43 1948

The study of the blind spot is considered to yield useful results in the diagnosis of early hypertension The author examined by campimetry 69 eyes in 35 patients with early hypertension Some control studies were carried out on normal eyes In 67 of the 69 eyes there were definite deviations from the normal which fell into two groups (1) significant increase in the extent of the blind spot (2) irregularities in its contours prolongations taking the shape of knobs teeth and attenuated branches Ophthalmoscopic examination revealed some changes in the fundus in 28 cases *S S B Gilder*

Ecchymosis of the Abdominal Wall as an Early Diagnostic Sign of Dissecting Aneurysm of the Aorta R. GREEN and O SAPHIR. *Amer J med Sci*, 216, 24–26 July, 1948

In a patient in whom the findings indicated acute embolic occlusion of the iliac artery, the presence of ecchymosis of the abdominal wall suggested the diagnosis of acute dissecting aneurysm of the aorta This was confirmed at necropsy, the ecchymosis resulting from involvement of the deep inferior epigastric arteries *T Semple*

Place of Intermittent Venous Hyperemia in the Treatment of Obliterative Vascular Disease M H EVOY and G DE TAKATS *Arch intern Med*, 81, 292–300 March, 1948

Intermittent venous hyperæmia is indicated after acute arterial occlusion if embolectomy or sympathectomy is not feasible or after either procedure as post-operative treatment, and in patients with chronic arterial occlusion due to arteriosclerosis with and without diabetes, to syphilis, or to thrombo-angiitis obliterans Patients with marked vasospasm, as in the earlier stages of thrombo-angiitis, are subjected by the authors to sympathectomy before the treatment is begun The procedure is contraindicated in acute venous thrombosis, lymphangitis, severe arteriolar obstruction, and in the presence of frank gangrene The treatment has been found useless for neuropathies, whether ischæmic or metabolic, causalgic states, and sequelæ of frost-bite and immersion foot

A hundred ambulatory patients with intermittent claudication and numbness and tingling of the toes, often associated with angina pectoris, were studied over a period of one year or more, the apparatus being used at home, 35 showed notable improvement with the treatment and 32 slight improvement. Improvement was measured by noting walking ability and venous filling times The rationale of the treatment is doubtful, but in addition to a small reactive hyperæmia a mechanical filling and stretching of the terminal vascular bed takes place during the procedure *T Semple*

Dicumarol Therapy in Acute Coronary Occlusion with Myocardial Infarction. M MCCALL. *Amer J med Sci*, 215, 612–616, June, 1948

From a study at the Beekman Downtown Hospital, New York, of 71 patients with proven coronary thrombosis the conclusion was reached that dicoumarol is a therapeutic agent of safety and value, it appears to be a preventive of thromboembolic phenomena in cases of acute coronary occlusion associated with myocardial infarction Prothrombin estimations are essential for safe therapy, but if in spite of these, hæmorrhagic complications such as hæmaturia occur, they will respond to intravenous administration of 60 mg. of menadione The dosage of dicoumarol is 300 mg. on the first day, with 200 mg, or less according to the prothrombin readings, daily for three or four weeks *G F Walker*

The Role of Thebesian Drainage in the Dynamics of Coronary Flow in Cases with and without Coronary Sclerosis P I HALONEN and A AHO *Acta path. microbiol scand*, 25, 567–572, 1948

Calf hearts and human hearts were perfused with saline and the amount of fluid reaching the various chambers was measured It was found that drainage into the right heart by way of the venæ Thebesii was quite considerable, and this fact thus lends support to the hypothesis that a reversal of blood flow in these veins may transform them into auxiliaries to the coronary arteries whenever these are narrowed or occluded No difference in Thebesian drainage was observed between normal hearts and those showing coronary sclerosis *R Salm*

Treatment of Angina Pectoris by Infiltration of Procaine Solution Around the Superior Cervical Ganglion K A. DRYAGIN *Klin Med, Mosk*, 26, No 5, 23–26, May, 1948

Infiltration of 30 ml of 0 25% procaine solution into the neighbourhood of the superior cervical ganglion gave unexpectedly good results in 24 cases of angina pectoris, in 19 the attack was arrested at once and in 3 pain was greatly relieved After 1 year, 8 out of 12 of these patients were still free from pain A second infiltration in cases of relapse was less effective No complications were observed *S S B Gilder*

Angiocardiography in the Diagnosis of Congenital Heart Disease K. D KEELE. *Brit J Radiol*, 21, 380–393, Aug., 1948

The author briefly reviews the history of angiocardiography, and describes the technique employed upon a number of children The patient was anæsthetized with cyclopropane and oxygen It was found that the best visualization was given by films taken in the left oblique position and in the supine antero-posterior position There were no untoward reactions The normal appearances are described and well illustrated by line drawings The author emphasizes that the cadaver appearance of the interior of the heart chambers is modified by the tendency to formation of an axial stream, by the presence of blood currents, and by dilution of the contrast medium

He describes 5 cases of congenital heart lesion These included 3 cases of patent ductus arteriosus, 1 accompanied by complete heart block, 1 by pulmonary stenosis, and 1 by a patent interauricular septum In one of these cases the communicating channel between pulmonary artery and aorta was visualized directly A case of coarctation of the aorta is well illustrated and the defect in the interventricular septum in a fifth case is clearly shown

In the author's view, when a lesion is present for which, on clinical grounds, surgery is the treatment of choice, angiocardiography is indicated, both for accurate diagnosis and to reveal any co-existing abnormalities *A M Rackow*

Regulation of the Circulation in Malnutrition H REINDELL and H KLEPZIG *Z ges inn Med*, **3**, 193–199, April, 1948

Undernourished men and women of all ages generally have a lowered systolic and diastolic blood pressure and a slowed heart rate The hypotension and bradycardia which appear before any gross intestinal disturbance (such as hunger œdema), are not the result of myocardial damage or of a disturbed circulatory control They are rather the expression of a special type of control for the sake of circulatory economy, and are associated with a diminished minute volume, a lessening of the elastic resistance, and an increase of the peripheral resistance

R T Grant

Circulatory Responses to Spinal and Caudal Anesthesia in Hypertension Relation to the Effect of Sympathectomy I Effect on Arterial Pressure R D TAYLOR, R BIRCHALL, A C CORCORAN, and I H PAGE. *Amer Heart J*, **36**, 221–225, Aug, 1948

Observations on 43 patients before and after operation lead to the conclusion that the blood-pressure response to spinal and caudal analgesia has no more than a negative value in the selection of patients for sympathectomy *R T Grant*

Circulatory Responses to Spinal and Caudal Anesthesia in Hypertension Relation to the Effect of Sympathectomy II Effect on Renal Function A C CORCORAN, R D TAYLOR, and I H PAGE *Amer Heart J* **36** 226–240, Aug, 1948

High spinal or caudal analgesia which materially reduces blood pressure in hypertensive patients usually causes renal vasodilatation, resulting in increased renal blood flow and a slight decrease in glomerular filtration rate This is inconsistent with the view that essential hypertension is a compensation for increased renal vascular resistance The renal vascular response to analgesia is not a positive guide to the selection of patients for sympathectomy *R. T Grant*

A Comparative Evaluation of Tetraethylammonium Chloride and Sodium Amytal in Patients with Hypertensive Cardiovascular Disease I G TAMACNA and C A POINDEXTER *Amer J med Sci*, **215**, 651–654 June, 1948

The effects on systolic and diastolic blood pressure of intravenous injection of tetraethyl-ammonium chloride and the standard sodium amytal test were compared in 68 hypertensive subjects Injections of 2 ml (0 2 mg) of tetraethyl ammonium chloride were given intravenously over a period of 1 to 1½ minutes and the blood pressure was recorded until the initial level was regained The lowest level was reached 1 to 3 minutes after the injection, and a smaller secondary fall was usual about 10 minutes after the injection There is a parallel fall in systolic and diastolic pressures In a comparison of the fall in the diastolic pressure in the two tests it was found that the difference was less than 15 mm in 51 cases, 15 to 30 mm in 13 cases and above 30 mm in 4 cases The largest discrepancies occurred in cases of malignant hypertension, the fall usually being greater with tetraethyl ammonium chloride Reactions were not important, but were most noticeable in patients with malignant hypertension

The authors regard the test as an advance on the sodium amytal test in the assessment of cases for sympathectomy in view of its greater convenience and on the theoretical grounds that tetraethyl ammonium chloride acts by blocking impulses at the sympathetic ganglia

J W Litchfield

Observations on Micro nodular Pulmonary Radiological Shadows Pulmonary Arterial Hypertension C LAUBRY J LENÈGRE and L ABBAS *Bull Soc méd Hop Paris* **64**, 741–749, June 1948

Fine nodular shadows disseminated throughout the lung fields in association with mitral stenosis are occasionally seen on radiological examination and have been described in Britain by Anglin Elkeles, and Gumpert Five further cases are here described and discussed and the literature reviewed The small hard shadows are characteristically most densely aggregated in the mid zones and there is a generalized fibre mesh appearance of the lung with marked hilar congestion The condition is seen most commonly in males between the ages of 20 and 40 with mitral stenosis and frequent hæmoptyses In one case histological examination at necropsy showed that the nodules consisted of masses of large heart failure cells full of iron pigment clumped together in the alveoli and their walls There was also much extracellular pigment It was previously thought that the nodules consisted merely of aggregations of heart failure cells due to capillary stasis but here the importance is stressed of repeated hæmoptyses and subsequent phagocytosis of the red blood corpuscles

F G Sita Lumsden

CARDIAC INFARCTION WITH BUNDLE BRANCH BLOCK

BY

W SOMERVILLE AND PAUL WOOD

From the Institute of Cardiology, London

When cardiac infarction is complicated by bundle branch block, the electrocardiogram may or may not show the features characteristic of myocardial injury Interference with conduction through the left branch of the bundle of His usually suppresses pathological Q waves and other RS–T segment or T wave changes in the standard and unipolar limb leads and in chest leads, it may then be impossible to make a cardiographic diagnosis of cardiac infarction When a conduction defect involves the right branch, however, cardiographic signs of cardiac infarction can, as a rule, still be recognized (Wilson et al, 1947)

The association of cardiac infarction and bundle branch block is not uncommon (Oppenheimer and Rothschild, 1917, Applebaum and Nicholson, 1935, Comeau et al, 1938, Fischer, 1938, Master et al, 1938, Moia and Acevedo, 1945) Since the majority of these reports were published, the use of multiple chest leads has permitted a higher degree of precision in the diagnosis of cardiac infarction and in the localization of intraventricular conduction defects, and it is likely that in the future the association of these two conditions will be diagnosed more frequently and with greater accuracy (Wilson et al, 1944) The subject is of considerable importance, not only from the viewpoint of practical diagnosis, but also because cardiac infarction complicated by bundle branch block has a mortality almost twice as great as that of infarction with normal intraventricular conduction (Master et al, 1938)

The object of this investigation was to determine the frequency with which the electrocardiographic signs of cardiac infarction could be recognized in the presence of bundle branch block and to discover what factors tended to prevent their suppression

MATERIAL

The electrocardiograms and case-notes that form the basis of this report were obtained from the records of Hammersmith Hospital, the London Hospital, and the National Heart Hospital The majority of the patients concerned, however, were examined and investigated by one or other of the writers A number of patients who had been under observation before the war could not be subsequently traced Follow-up studies are therefore incomplete

Generally the diagnosis of cardiac infarction was based on a typical clinical history, when this was lacking, the diagnosis depended on X-ray evidence of ventricular aneurysm or on the demonstration of an infarct at necropsy Bundle branch block was recognized according to the criteria laid down by Wilson and his co-workers, namely —

" when the QRS interval measures 0 12 second or more and the QRS complex in lead I is monophasic and consists of a broad, slurred, flat-topped or bifid deflection, left bundle branch block is usually present When the QRS interval measures 0 12 second or more and the QRS complex in lead I is biphasic or triphasic and ends with a broad, slurred or notched S deflection the block is usually in the right bundle When the heart is in the vertical position the limb leads may suggest that right branch block is present when the præcordial curves are characteristic of left branch block, and vice versa When the QRS interval measures 0 12 second or more and the præcordial electrocardiogram shows some but not all of the features typical of right or left branch block the conduction defect cannot be located with certainty " (Wilson et al, 1944)

RESULTS

The present series consisted of 60 cases of cardiac infarction and bundle branch block, and was divided into two groups depending on whether the electro-

cardiogram revealed evidence of both cardiac infarction and bundle branch block, or of bundle branch block only   The composition of the two groups is presented in Table I

The main features of the 41 cases showing cardiographic evidence of both cardiac infarction and bundle branch block are set down in Table II

CARDIAC INFARCTION AND LEFT BUNDLE BRANCH BLOCK

There were 33 cases with a clinical history of cardiac infarction and an electrocardiogram showing left bundle branch block   In sixteen of these (48 per cent) the cardiogram also revealed abnormal Q waves, RS–T segment deviations, or altered T waves characteristic of cardiac infarction

The relative frequency of such signs in the various leads taken are set down in Table III (anterior infarction) and Table IV (posterior infarction)

Anterior Infarction

In experiments on dogs, Wilson and his co-workers have shown that when the left branch of the bundle of His is interrupted, direct leads from the epicardial surface of a left ventricular transmural infarct record the initial positive potential of the left ventricular cavity and therefore cannot show a Q wave   When the infarct includes the ventricular septum, however, the initial negative potential of the endocardial surface of the right ventricle may be transmitted through the infarcted—and hence electrically inert—septum to the cavity of the left ventricle   Then leads facing the left ventricular surface may show an initial negative deflection (Q wave) characteristic of cardiac infarction (Wilson *et al*, 1944, Sodeman *et al*, 1944)

In all but one of the 12 cases in which a cardiographic diagnosis of anterior infarction was made, a Q wave was present in lead I and in leads taken over the left præcordium (Fig 1)   A similar change was found in the unipolar left arm lead (VL) in five of the six cases in which it was taken   When present in the left præcordial leads, Q may be expected in leads I and VL, but cannot be guaranteed (Wilson, 1936, Master *et al*, 1938)   Septal infarction was found in all three of our cases of left bundle branch block with a Q in lead I that were examined post-mortem

RS–T segment deviation in greater or less degree and abnormal T waves usually accompanied abnormal Q waves (Fig 2), only one example (Case 2) was encountered where a diagnosis of infarction could be made from the RS–T segment or T wave in the absence of a Q wave   Marked RS–T segment elevation and coving is a feature of fresh infarction with left bundle branch block as well as with normal conduction (Bach, 1930, Master *et al*, 1938, Vela, 1944, Moia and Acevedo, 1945, and others) and has been demonstrated experimentally in animals (Hill, 1934)   For a time it may be the only clear sign of infarction, preceding the appearance of Q, or the latter may be indistinct or fail to develop   It follows that if an electrocardiogram can be obtained within a few hours or days of infarction, a cardiographic diagnosis of infarction will be possible in a correspondingly higher proportion of cases despite the left bundle branch block   As a rule, however, the RS–T segment depression in lead I typical of left bundle branch block tends to neutralize the RS–T elevation of anterior infarction, and this segment is usually isoelectric or only slightly elevated or depressed (Fig 2)   RS–T segment elevation is not necessarily confined to the

TABLE I

ELECTROCARDIOGRAPHIC FINDINGS IN 60 CASES OF BUNDLE BRANCH BLOCK WITH HISTORY OR OTHER EVIDENCE OF CARDIAC INFARCTION

| Electrocardiogram | Sex | | Age (av) | Left bundle branch block | | | | Right bundle branch block | | | |
	Male	Female		Ant	Post	Ant and post	Total	Ant	Post	Ant and post	Total
Cardiac infarction and bundle br block (41 cases)	35	6	60	12	4	0	16	14	10	1	25
Bundle br block only (19 cases)	15	4	63	—	—	—	17	—	—	—	2
Total (60 cases)	50	10	61 5	—	—	—	33	—	—	—	27

TABLE II

CASES OF CARDIAC INFARCTION SHOWING ELECTROCARDIOGRAPHIC EVIDENCE OF BOTH CARDIAC INFARCTION AND BUNDLE BRANCH BLOCK

Case No	Sex	Age	Date of infarct	Date of electro-cardio-gram	Electrocardiogram					Site of infarct at necropsy[3]
					Leads taken[2]	QRS (sec)	Abnormal Q	Deviation of RS-T	Abnor-mal T	
					Left Bundle Branch Block Anterior Infarction					
1	M	60	Indef	27/1/37	No chest leads	0 44	I		I	Antero-septal
2	M	53	10/11/47	13/11/47	VL, VR, VF V5, V3, V1	0 12		I, III VL V5	I VL V5	
3	F	69	Jan. 1945	5/1/48	CR7-1	0 12	I CR5-2	II CR6-2	I II CR7-2	
4	F	61	7/5/46	8/5/46	V5, V3, V1	0 12	I V3	V5, V3, V1	I V5, V3	
5	M	60	13/11/46	13/5/47	VL, VR, VF V6-1	0 16	I VL V5	V6-3	I VL	
6	M	73	26/12/46	28/12/46	V5, V3, V1	0 12	I V5 V3, V1	V5, V3	I	
7	M	33	July 1944	4/2/47	VL, VR, VF V5, V3, V1	0 12	I, II VL V5		I, II VL V5	
8	M	40	July 1947	17/11/47	VL, VR, VF V6-1	0 12	I VL V6-5		I VL V6-4	Antero-septal
9	M	57	Indef	5/4/45	IV R	0 12	I, II IV R		I, II	
10	M	68	(a) 6/4/47[1] (b) 5/10/47 (c) 10/1/48	10/1/48	VL, VR, VF V5, V3, V1	0 12	I VL V5	V5	I	Ant (recent) Post (old) I–V septum (recent and old)
11	M	59	Indef	10/2/48	V6, IV, V, V2, V1	0 16	I, II V6-5		I V6	
12	M	45	25/2/48	25/5/48	aVL, aVR, aVF V6-1	0·12	I VL V6-3	IVV, V2, V1 I V6-3	V6	
					Left Bundle Branch Block Posterior Infarction					
16	M	62	Indef	2/8/46	CR7, CR4	0 12	II, III CR7, CR4	III	III	
17	F	45	23/11/46	27/11/46	V5, V3, V1	0 12	III	III	III	
18	F	59	(a) Aug 47[1] (b) 20/1/48	22/1/48	VL, VR, VF V5, V3, V1	0 14	II, III VF	I II, III VL, VF V5³	II, III VF	
19	M	60	3/9/47	9/9/47	VL VR, VF V5 V3, V1	0 12	II, III VF	I, II, III V5·	II, III VI⁶ VF	
					Right Bundle Branch Block Anterior Infarction					
20	M	63	(a) Jan 1946 (b) 25/2/47 (c) 27/2/47	25/2/47	V5, V3, V1	0 12	V5 V3, V1	V5, V3		Antero-sep-tal (recent) Posterior (old)
21	M	81	29/11/47	10/12/47	VL, VR, VF V5, V3 V1	0 12	V3 V1	V3	V5, V3	Antero-sep-tal (recent) Posterior (old)

TABLE II—*continued*

Case No	Sex	Age	Date of infarct	Date of electrocardiogram	Electrocardiogram					Site of infarct at necropsy[3]
					Leads taken[2]	QRS (sec.)	Abnormal Q	Deviation of RS-T	Abnormal T	
					Right Bundle Branch Block Anterior Infarction—continued					
[1]22	M	56	20/12/35	21/12/35	IVR, CR2, CR1	0 16	CR2-1	IV R CR2-1	IV R CR2-1	
[1]23	M	81	Indef	29/9/46	V5, V3, V1	0 16	I V5, V3, V1	V5	V3	Antero-sep-tal
24	M	79	(a) 3/9/36 (b) Oct 1936 (c) 14/11/36	15/1/48	VL, VR, VF V6-1	0 16	I VL V6-1	V3-1	V6-1 I	
25	M	58	Indef	23/3/44	IV R	0 14	I		IV R I	
26	M	61	May 1937	July 1937	No chest leads	0 12	I		I	
27	M	54	16/5/47	25/9/47	VL, VF V5, V3, V1	0 14	V3, V1		V3, V1	
[1]28	M	59	Indef	8/4/48	VL, VR, VF V5, V3, V1	0 16	I VL V5, V3, V1	I V5, V3	V3, V1	Antero-sep-tal
29	M	39	24/12/47	6/4/48	VL, VR, VF V5, V3, V1	0 16	I VL V5, V3	VL V5	V5	
[1]30	M	51		5/4/48	aVL, aVR, aVF V7-1, V3R	0 12	aVL V5-1 V3R	I aVL V3		Antero-sep-tal (recent) Posterior (old)
31	M	55	21/4/48	12/5/48	V5, V3 V1	0 12	V1			
32	M	77	10/12/47	13/1/48	VL VR, VF V6-1	0 16	I VL V5-2			
33	M	63	29/3/48	3/5/48	VL, VR, VF V5, V3, V1	0 16	I VL V5, V3	V3		
					Right Bundle Branch Block Posterior Infarction					
40	M	61	(a) 1940 (b) 27/7/43	8/1/48	CR7-1	0 16	II, III	II III	II III	
41	F	69	Jan 1938	7/3/38	No chest leads	0 16	II III	III	II, III	
42	M	51	4/9/46	25/9/46	CR7, CR4, CR1	0 12	II III	III	III	
43	M	67	Oct 1947	12/12/47	VL VR, VF V7-1	0 14	II III VF	III VF	II III VF	
44	F	64	(a) Feb 1946 (b) 28/6/46	9/8/46	CR7, IV R	0 16	II, III	II, III	II III	
45	M	61	Indef	17/2/41	IV R	0 12	II, III	II, III	II	
[1]46	M	67	(a) May '45 (b) 5/10/47	9/7/45 11/10/47	No chest leads CR7, CR4[7]	0 14 0 12	II III III	II III	II III CR7	
47	M	45	Feb 1945	18/7/47	CR7, CR3 CR2	0 14	II III CR7	II, III	II III	
48	M	54	12/12/47	13/2/48	CR7-1	0 14	II III	II III	II III	
[1]49	M	52	15/3/44	20/3/44	IV R, CF2	0 16	II, III	IV R[8]		Anterior, posterior and septal
50	M	68		24/3/48	VL, VR, VF V6-1	0 12	II III VF			

[1] Dead   [2] Standard limb leads were taken in all cases   [3] 'Anterior and Posterior refer to left ventricle
[4] Electrocardiogram showed posterior infarction with normal intraventricular conduction
[5] Marked depression of RS–T segment   [6] Abnormally tall T waves present in lead VI
[7] Left bundle branch block   [8] In IV R, QRS and RS–T segment indicated involvement of apical region

TABLE III

ELECTROCARDIOGRAPHIC SIGNS OF ANTERIOR INFARCTION
COMPLICATED BY LEFT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (12 cases)	
11	3	11
	Chest leads (10 cases)	
9	8	6
	Unipolar limb leads (6 cases)	
5	1	4

TABLE IV

ELECTROCARDIOGRAPHIC SIGNS OF POSTERIOR INFARCTION
COMPLICATED BY LEFT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (4 cases)	
4	4	4
	Chest leads (4 cases)	
1	2	1
	Unipolar limb leads (2 cases)	
2	1	2

acute stages of the infarct but may persist for months or years In eight of our twelve cases in this group, prominent RS–T elevation in lead I and/or the left chest leads was present for 2 days (Case 10), 9 days (Case 4), 2 weeks (Cases 2 and 6), 2–3 months (Cases 11 and 12), and 6 months (Case 5) In the eighth case conspicuous RS–T segment deviation was still evident in leads CR5–2 three years after the infarct (Fig 3A) and in Case 11 in leads V4–2 five years after the infarct (Fig 3B) Persistent RS–T deviation has been described as a sign of cardiac aneurysm (Nordenfelt, 1939, Wilson et al, 1944b), but this could not be detected in any of our cases

Primary T wave changes associated with anterior cardiac infarction usually cannot be recognized in the presence of left bundle branch block, for the latter produces strong T wave inversion in lead I and in leads taken over the left ventricle In no case did we feel justified in making a diagnosis of cardiac infarction by virtue of T wave changes alone

Care must be taken in interpreting chest lead curves taken from positions C1 and C2 in uncomplicated left bundle branch block since these leads
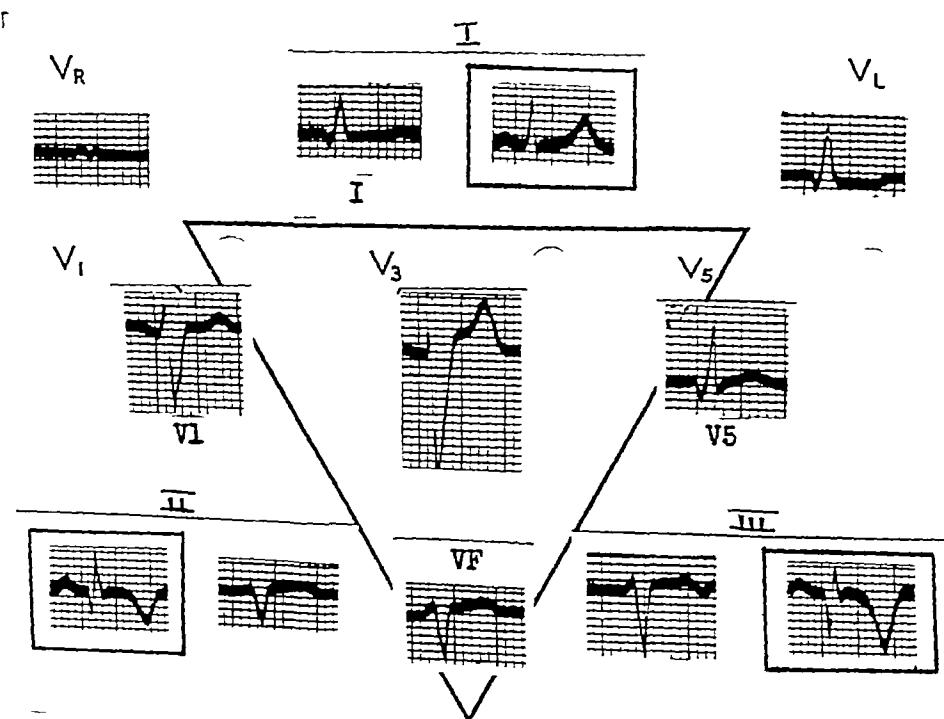
FIG 1 —Anterior cardiac infarction and left bundle branch block Previous standard leads, outlined in black, show the original posterior infarct A prominent Q wave due to involvement of the septum is seen in lead V5, and is transmitted to lead VL and to standard lead I Autopsy confirmation
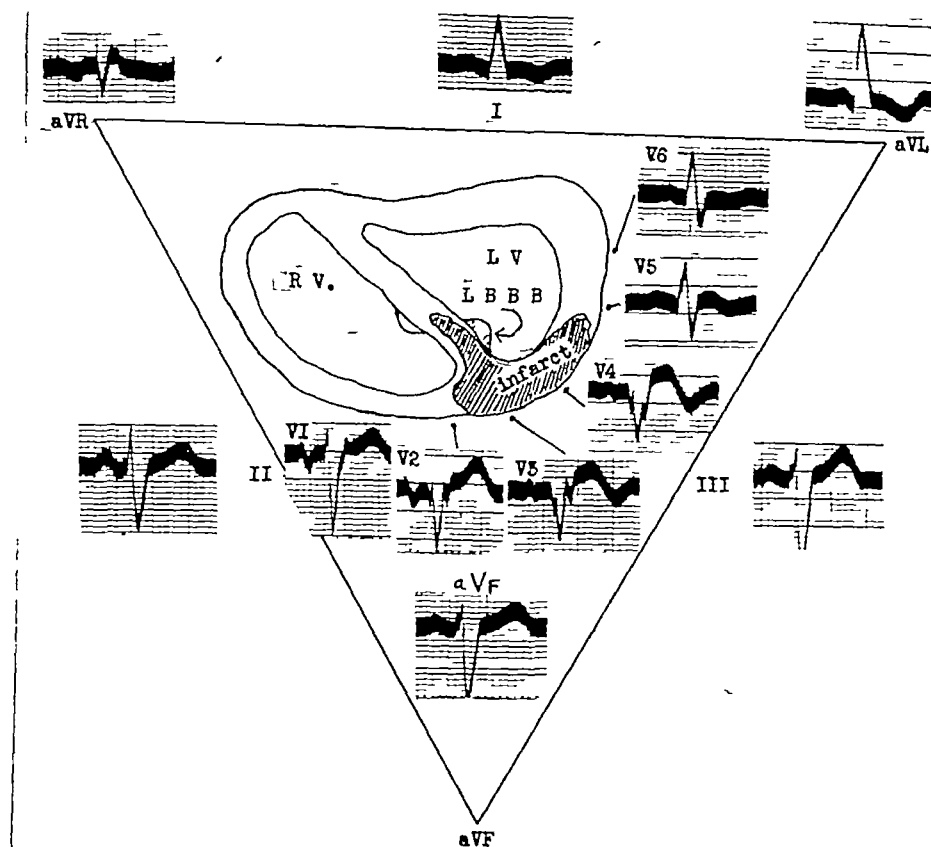
FIG 2 —Anterior cardiac infarction and left bundle branch block Elevation of the RS–T segment due to the infarct, seen best in leads V3 and V4 neutralizes any tendency towards RS–T depression due to left bundle branch block thus in leads VL and standard lead I the RS–T segment is at the isopotential level The small Q wave in these two leads is due to septal infarction Autopsy confirmation

may show an inconspicuous R wave or may consist of a monophasic downward deflection followed by an elevated RS–T segment more or less simulating recent anterior or antero septal infarction Such complexes are sometimes known as " false infarction curves " (Mortensen, 1940)

Convincing evidence that left bundle branch block may suppress the signs of infarction was obtained in certain cases in which the block was transient (Fig 4), or intermittent (Fig 5)

Cardiographic signs of cardiac infarction obscured by left bundle branch block may be unmasked when a premature ventricular contraction originating on the blocked side allows both ventricles to contract simultaneously Wilson and Herman (1921) were able to demonstrate the presence of an infarct in the experimental animal by this means and explained

the physiological mechanism We have encountered several examples of this type and others have been reported (Dressler, 1943, Simonson et al, 1945)

Posterior Infarction

When posterior infarction is complicated by left bundle branch block the appearance of characteristic Q waves depends as in anterior infarction, on the transmission of the initial negative potential of the right ventricular cavity through an infarcted ventricular septum to the cavity of the left ventricle This initial negativity is then transmitted through the electrically inert posterior infarct to lead VF and so to leads II and III But QIII is also seen in at least one-third of cases of uncomplicated left bundle branch block (Sodeman et al 1944)

In the four examples of posterior infarction that
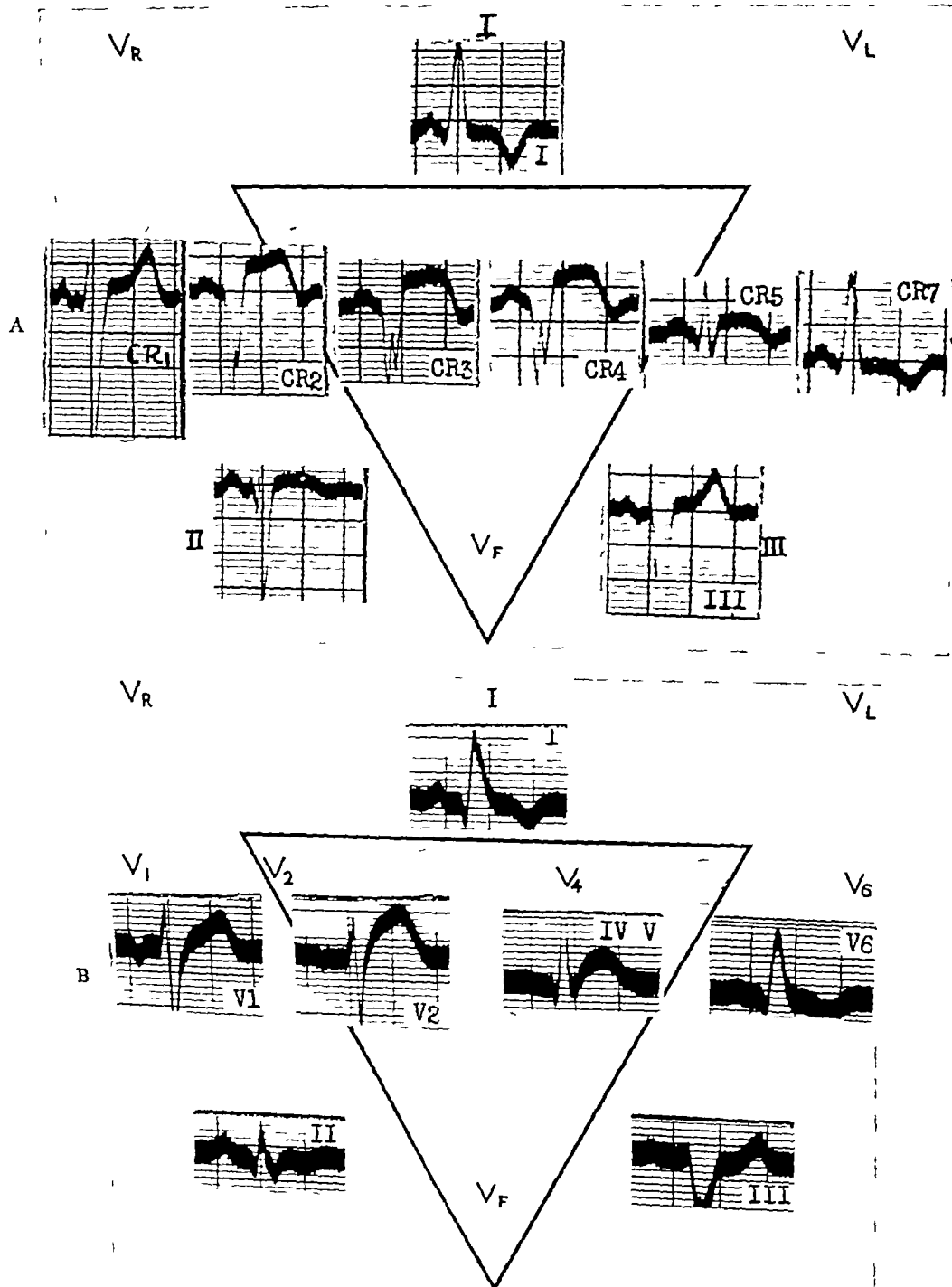
Fig 3 —Anterior infarct and left bundle branch block showing persistent elevation of the RS–T segment—three years after the infarct in example (A), and five years after the infarct in example (B) best shown in leads CR4 and V4 respectively   The Q wave in left ventricular surface leads or their equivalents in both cases is due to septal infarction
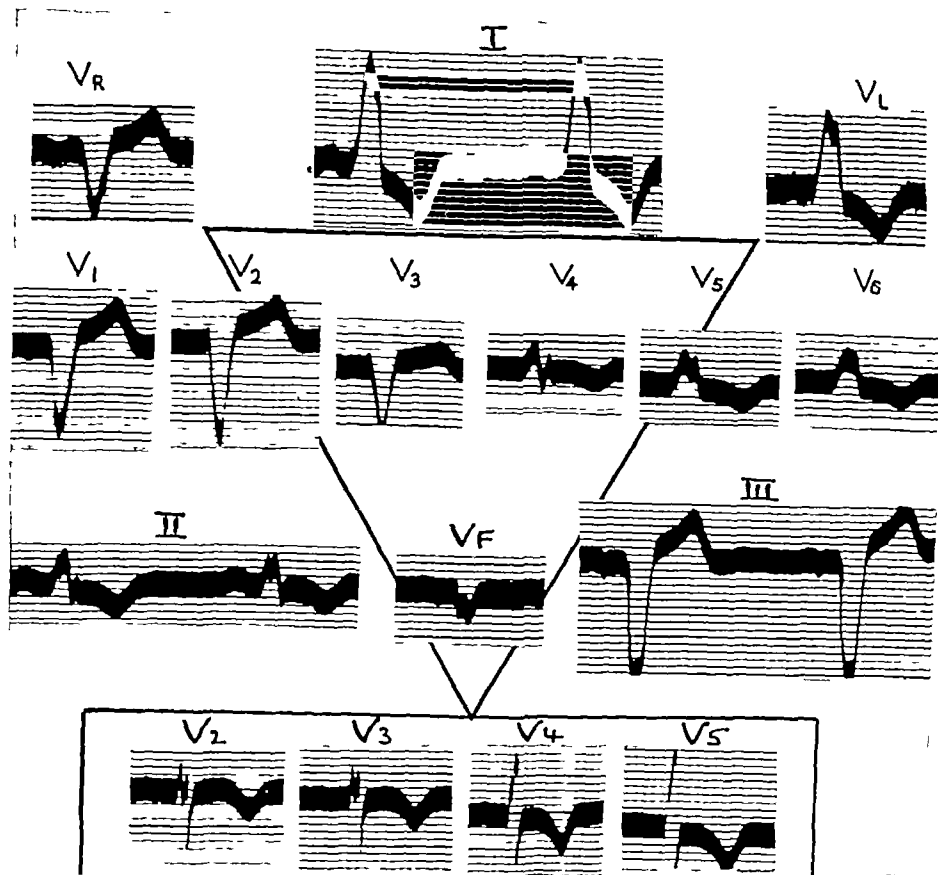
FIG 4 —Transient left bundle branch block suppressing the signs of anterior cardiac infarction
When conduction was normal (shown below) the T waves were inverted from V2 to V5

could be diagnosed cardiographically in this series, characteristic Q, RS–T, and T wave changes occurred in lead III   In one instance the curves were taken within a few hours of the onset and revealed RS–T segment elevation in leads II, III, and VF, with reciprocal depression in leads I, VL, and V5 (Fig 6) Proof of septal involvement in these cases is lacking, three of them recovered, and the fourth did not come to necropsy   On the other hand, extensive posterior infarction not involving the septum was demonstrated at necropsy in Case 75   The cardiogram (standard limb leads and IV R) showed left bundle branch block without the signs of posterior infarction

Comment

When the different factors are evaluated that tend to permit or suppress the signs of infarction complicated by left bundle branch block, which are discussed below, one may conclude tentatively

that in about one-half of such cases cardiographic confirmation of the infarction will be forthcoming, in the other half, as long as the bundle branch block persists, the cardiographic signs of infarction will be suppressed   The diagnosis must then depend on the history and other clinical evidence

CARDIAC INFARCTION AND RIGHT BUNDLE BRANCH BLOCK

When right bundle branch block is present the sequence of depolarization of the ventricles is the same as when intraventricular conduction is normal At the start of ventricular excitation the left ventricular cavity is negative and an infarct should transmit this initial negative potential to the surface in the usual way   Therefore the characteristic Q wave of cardiac infarction should not be suppressed

In our series there were 27 cases of cardiac infarction complicated by right bundle branch block
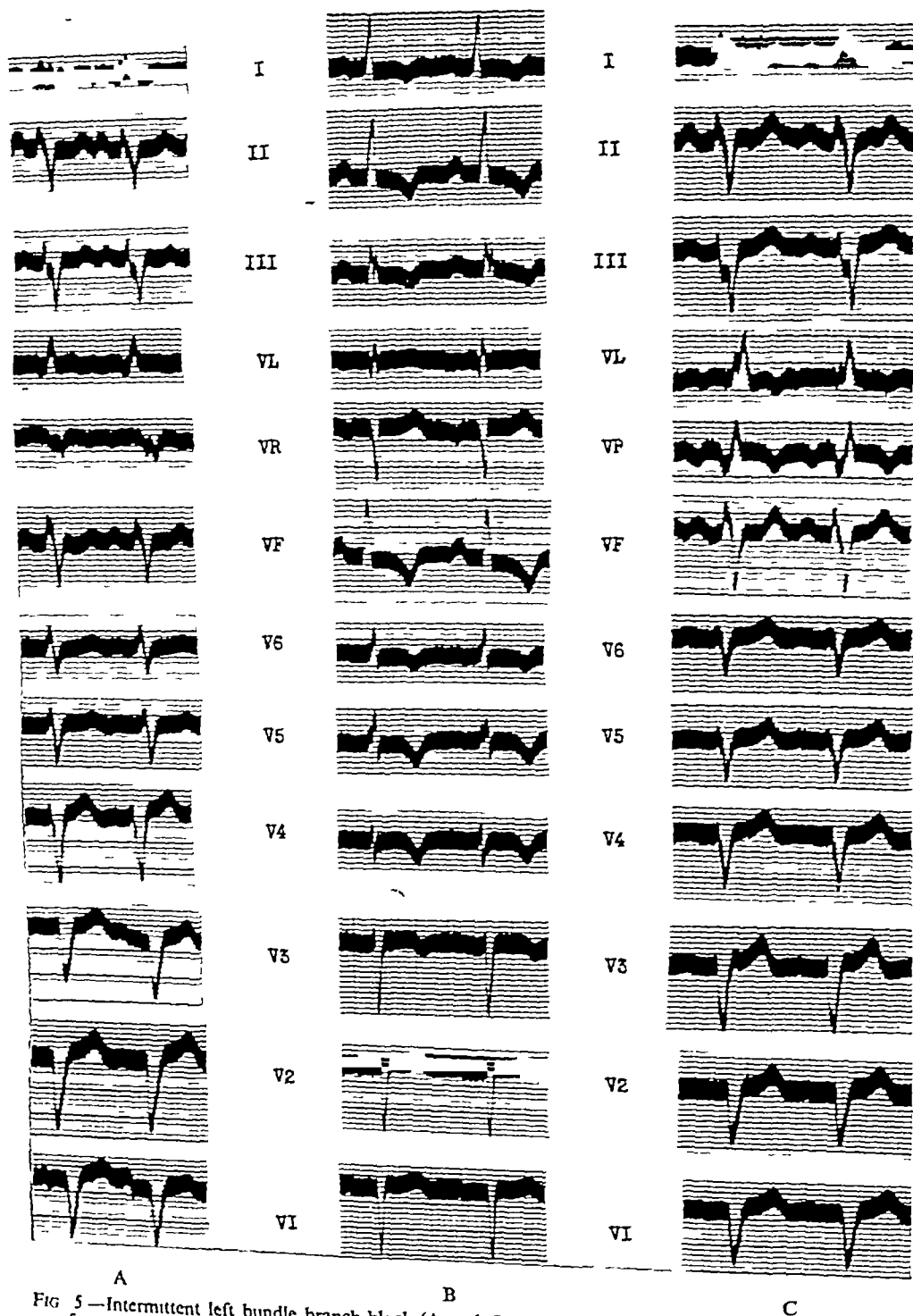
FIG 5 —Intermittent left bundle branch block (A and C) suppressing the signs of anterior cardiac infarction. When conduction was normal (B), primary T wave inversion of coronary type was seen from V3–V6 As the heart is electrically vertical, this inversion is transmitted to lead VF and hence to all standard leads
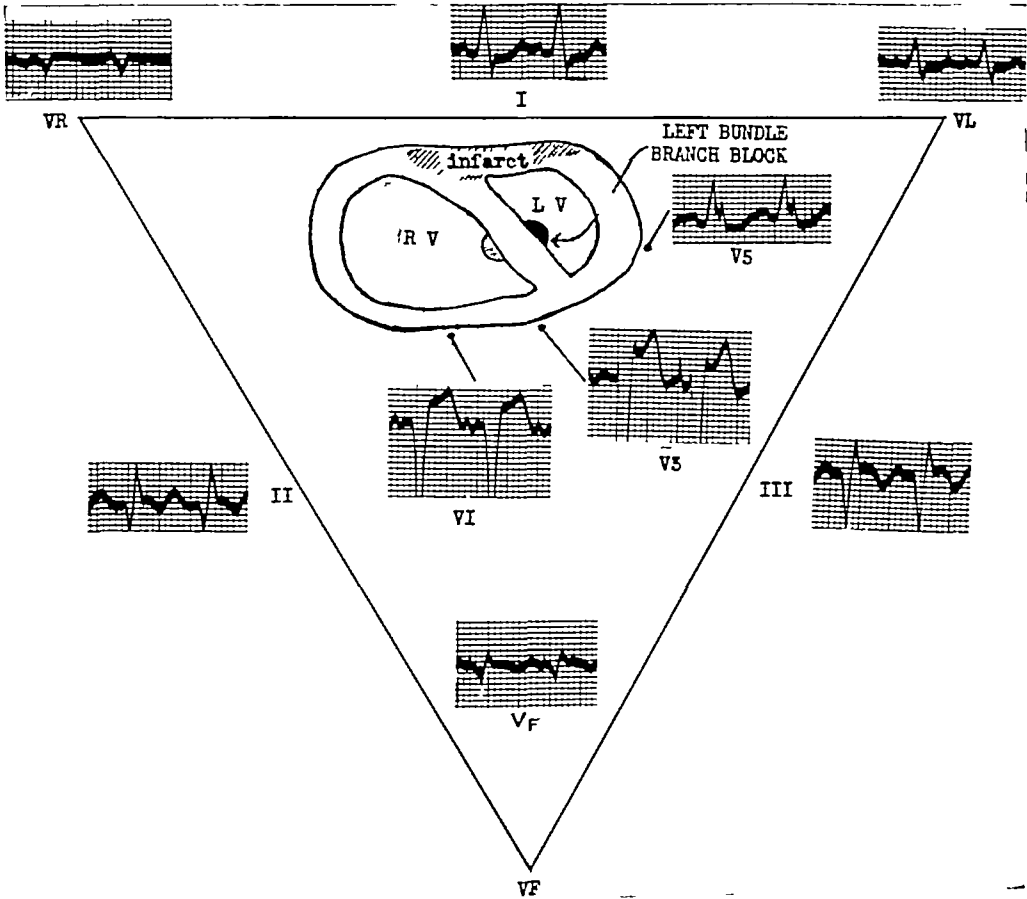
Fig 6 —Posterior cardiac infarction and left bundle branch block   This graph was taken within a few hours of the onset and shows characteristic changes denoting recent posterior infarction

The cardiographic signs of cardiac infarction were present in 25 cases, i e in 93 per cent   The relative frequency of these signs in the various leads taken is shown in Table V (anterior infarction) and Table VI (posterior infarction)   In six cases the infarct was confirmed at necropsy

TABLE V

ELECTROCARDIOGRAPHIC SIGNS OF ANTERIOR INFARCTION COMPLICATED BY RIGHT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
Standard limb leads (14 cases)		
8	2	1
Chest leads (12 cases)		
12	9	7
Unipolar limb leads (8 cases)		
6	2	0

TABLE VI

ELECTROCARDIOGRAPHIC SIGNS OF POSTERIOR INFARCTION COMPLICATED BY RIGHT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
Standard limb leads (11 cases)		
10	9	9
Chest leads (9 cases)		
1	1	1
Unipolar limb leads (2 cases)		
2	1	1

ANTERIOR INFARCTION

Eight of the fourteen cases of anterior infarction showed characteristic Q waves in the standard limb leads (Fig 7)   This is contrary to the experience of Wilson et al (1944), Carlotti (1947) and of Goldberger (1947)   RS–T segment deviation and
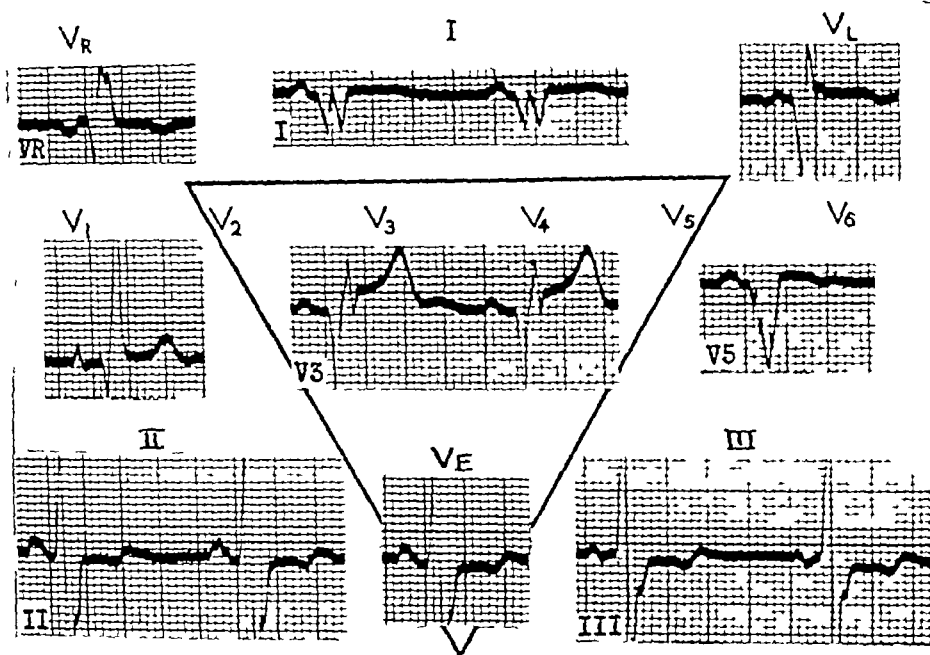
FIG 7—Anterior cardiac infarction and right bundle branch block   Typical Q waves are seen in leads V3, V5, VL and standard lead I

primary T wave changes were commonly absent from the standard limb leads thus in the six cases showing no Q I, these leads failed absolutely to show the infarct (Fig 8 and 10)

Multiple chest leads were diagnostic of infarction in the twelve cases in which they were recorded, Q waves being invariably present, and RS–T and T wave changes occurring in the majority (Fig 9)

The unipolar left arm lead reproduced the Q wave of anterior infarction in six out of eight cases (Fig 9) RS–T and T wave changes were seldom diagnostic

In Case 22 (Fig 10A) no cardiographic evidence of infarction was present six hours after an attack typical of coronary thrombosis On the following day right bundle branch block (QRS interval measuring 0 16 sec) had developed, evidence of infarction was then obvious in the chest leads but not in the limb leads The next record, taken nine days later when normal intraventricular conduction had returned, showed the pattern of anterior or antero-septal infarction in lead I and in the chest leads Serial cardiograms during the next fourteen months revealed gradual reversion towards normal, but monophasic negative initial ventricular complexes persisted in leads CR2 and CR1

The cardiogram shown in Fig 10B was taken a few hours after the onset of a prolonged attack of cardiac pain in a man aged 63 (Case 20) and dis-

closed right bundle branch block Diagnostic evidence of extensive anterior infarction was provided by chest leads, but not by limb leads At necropsy there was a recent infarct involving a large area of the anterior wall of the left ventricle and of the ventricular septum, and an old posterior infarct

The chest leads in Case 23 (Fig 11A) showed prominent Q waves in leads V5, V3, and V1, in addition to the features of right bundle branch block The complex recorded over the right præcordium (V1) resembled that in lead I, while V5 resembled lead III Therefore, the heart was electrically vertical At necropsy a recent infarct was found involving the apex and the lower portion of the ventricular septum The explanation of the tall R waves following deep Q waves seen in chest leads in cases of anterior infarction associated with right bundle branch block is obscure, because as Goldberger has pointed out (1947), the deep Q wave indicates that the lead in question is facing the infarcted left ventricle, whereas the tall R wave ordinarily occurs in leads that face the epicardial surface of the right ventricle in right bundle branch block

The cardiograms reproduced in Fig 11B (Case 21) are those of an old man of 81 who developed symptoms of cardiac infarction eleven days previously The unipolar limb leads showed the heart
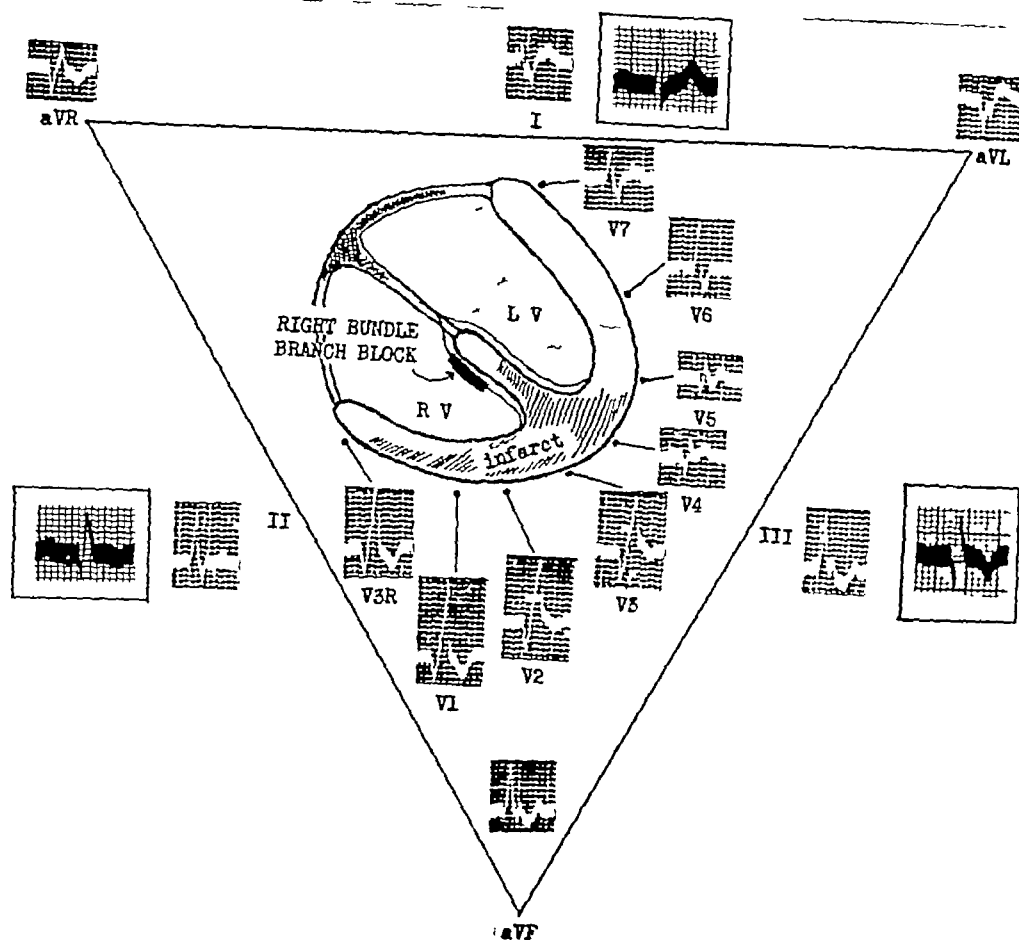
FIG 8 —Anterior cardiac infarction and right bundle branch block Typical Q waves are seen in the chest leads but the standard leads reveal no evidence of the infarct Standard leads outlined in black were taken previously and represent old posterior infarction Autopsy confirmation

to be electrically vertical, and the chest leads pointed to a block in the right bundle branch Conspicuous deviation of the RS–T segment was seen in lead V3 and small Q waves were present in this lead and in lead V1 The diagnosis was, therefore, right bundle branch block complicating an antero-septal infarct The patient died a week later and at necropsy this diagnosis was confirmed In addition an old posterior infarct was demonstrated

Posterior Infarction

When posterior infarction was associated with right bundle branch block, standard limb leads showed characteristic changes in all 11 cases (Fig 12) Unipolar limb leads were obtained in

only two instances (Cases 43 and 50) lead VF showed significant Q waves in both, with elevation of the RS–T segment and inversion of the T wave in one of them Multiple chest leads were taken in 9 cases, but revealed evidence of infarction in only one instance

When the posterior wall of the left ventricle is infarcted, and normal intraventricular conduction is present, the T wave in lead CR7 is usually inverted (Evans and Hunter, 1943) Although there is no apparent reason why a complicating right bundle branch block should suppress the characteristics of posterior infarction in this lead, an upright T wave was present in lead CR7 in five cases, and in V7 in a fourth (Fig 12 and 13B) The T wave in CR7 was
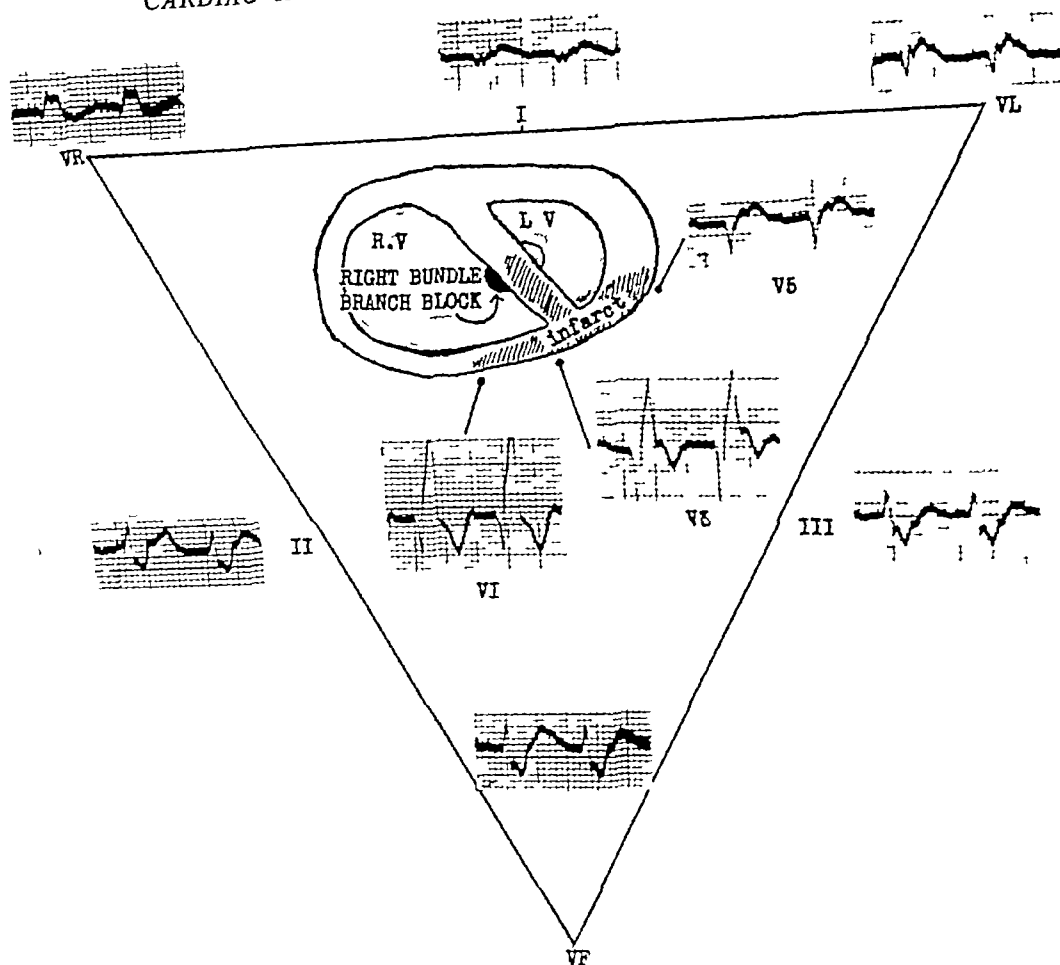
FIG 9 —Anterior cardiac infarction and right bundle branch block   Characteristic Q waves and RS–T elevation
are seen in V3, V5, VL and standard lead I   Autopsy confirmation

inverted in the fifth case (Fig 13A)   All these
records showed indubitable evidence of posterior
infarction in other leads

Some cases with widened and bizarre QRS com-
plexes are the result of fresh infarction distorting
the cardiogram of a previous bundle branch block
with or without infarction   Alternation of the
block between the left and right bundle branches
may occur (Master et al, 1938) or the pattern may
change permanently from one type of block to
another   In this respect Case 46 is of interest
A cardiogram taken in July 1945 showed right bundle
branch block with a posterior infarct   Two and a
half years later, after another attack of prolonged
cardiac pain, from which the patient did not recover,
a cardiogram showed left bundle branch block
(Fig 13B)   There was no necropsy

Occasionally, cardiographic evidence of posterior
infarction appears to be suppressed by right bundle
branch block   This occurred in Case 76, in which
the cardiogram showed right bundle branch block
with no more than a shallow Q wave in lead III,
yet at necropsy the posterior wall of the left ventricle
was found to be thinned and fibrosed over a large
area   The ventricular septum was not significantly
involved   The circumstances that result in sup-
pression of the signs of posterior infarction with
right bundle branch block are not clear   We did
not feel that a cardiographic diagnosis of infarction
could be based on an isolated Q wave in lead III,
because this is encountered in 36 per cent of cases of
uncomplicated right bundle branch block (Sodeman
et al, 1944)
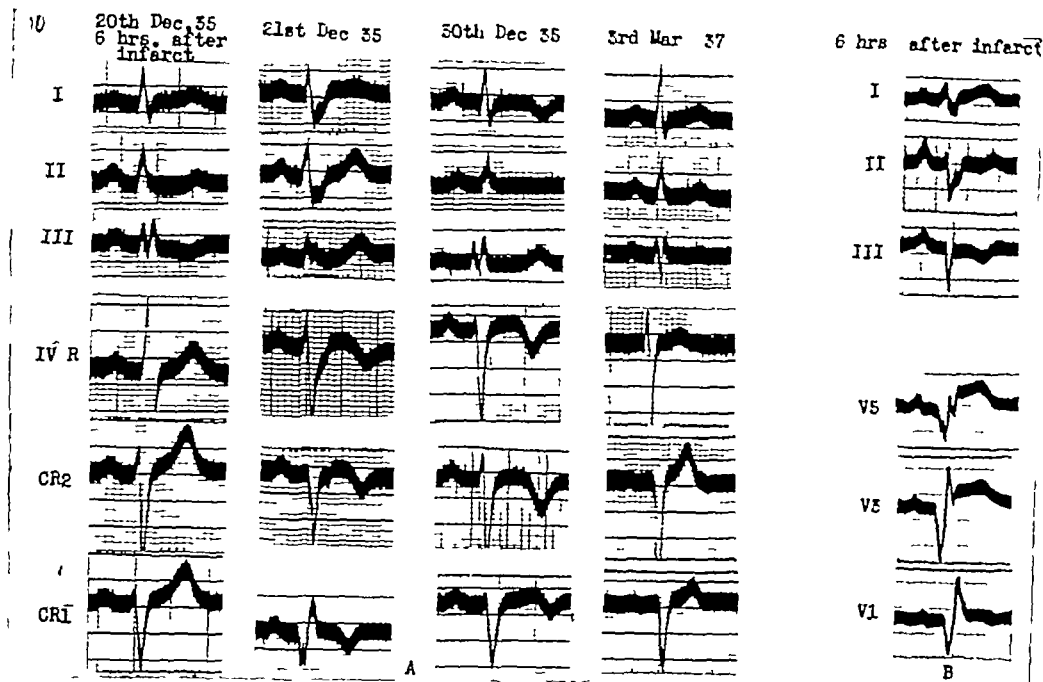
FIG 10 —Anterior cardiac infarction and right bundle branch block (A) Serial electrocardiograms showing the development of T wave changes characteristic of anterior infarction these are masked in standard leads when right bundle branch block is fully developed (December 21) (B) Typical changes of acute anterior infarction are seen in chest leads, but are masked by right bundle branch block in standard leads Autopsy confirmation

ANTERIOR AND POSTERIOR CARDIAC INFARCTION COMPLICATED BY BUNDLE BRANCH BLOCK

Necropsy evidence of anterior and posterior cardiac infarction was available in five cases in this series, three of them complicated by right and two by left bundle branch block In four of them the electrocardiogram showed signs of anterior or antero septal infarction only, three of these had right (Fig 8 and 11B), and the fourth left bundle branch block (Fig 1) The anterior infarct in each of these four cases was recent and the posterior infarct old In the fifth (Fig 14) a cardiogram taken six hours after the symptoms of a cardiac infarction showed normal intraventricular conduction with Q waves and depressed S–T segments in leads II and III, and abnormally tall T waves in the chest leads Five days later, left bundle branch block had developed, as shown in lead CF2 as the heart was vertical, standard leads resemble right bundle branch block A lead taken over the apex (IV R) was typical of acute anterior infarction An ante mortem diagnosis of recent anterior infarction in a vertical heart was made but at necropsy posterior infarction was also present

Thus, in these five cases the features of the acute infarct were revealed in the electrocardiogram, and in four of them the signs of an old posterior infarct were suppressed We have insufficient data, however, to determine the circumstances that result in the dominance of one infarct and the suppression of another

PATHOGENESIS OF BUNDLE BRANCH BLOCK COMPLICATING CARDIAC INFARCTION WITH AN ACCOUNT OF ELEVEN NECROPSIES

It is reasonable to assume that infarction of the ventricular septum might be associated with bundle branch block because of the intimate anatomical relationship between the septum and the bundle branches In the experimental animal septal infarction and usually bundle branch block with or without auriculo-ventricular conduction defects may be produced by ligation of the septal artery or of the left coronary artery (Wilson et al 1944) but the production of bundle branch block by this technique is sometimes unsuccessful (Barton and Greenwood 1933) In man the findings are similar When bundle branch block complicates cardiac infarction
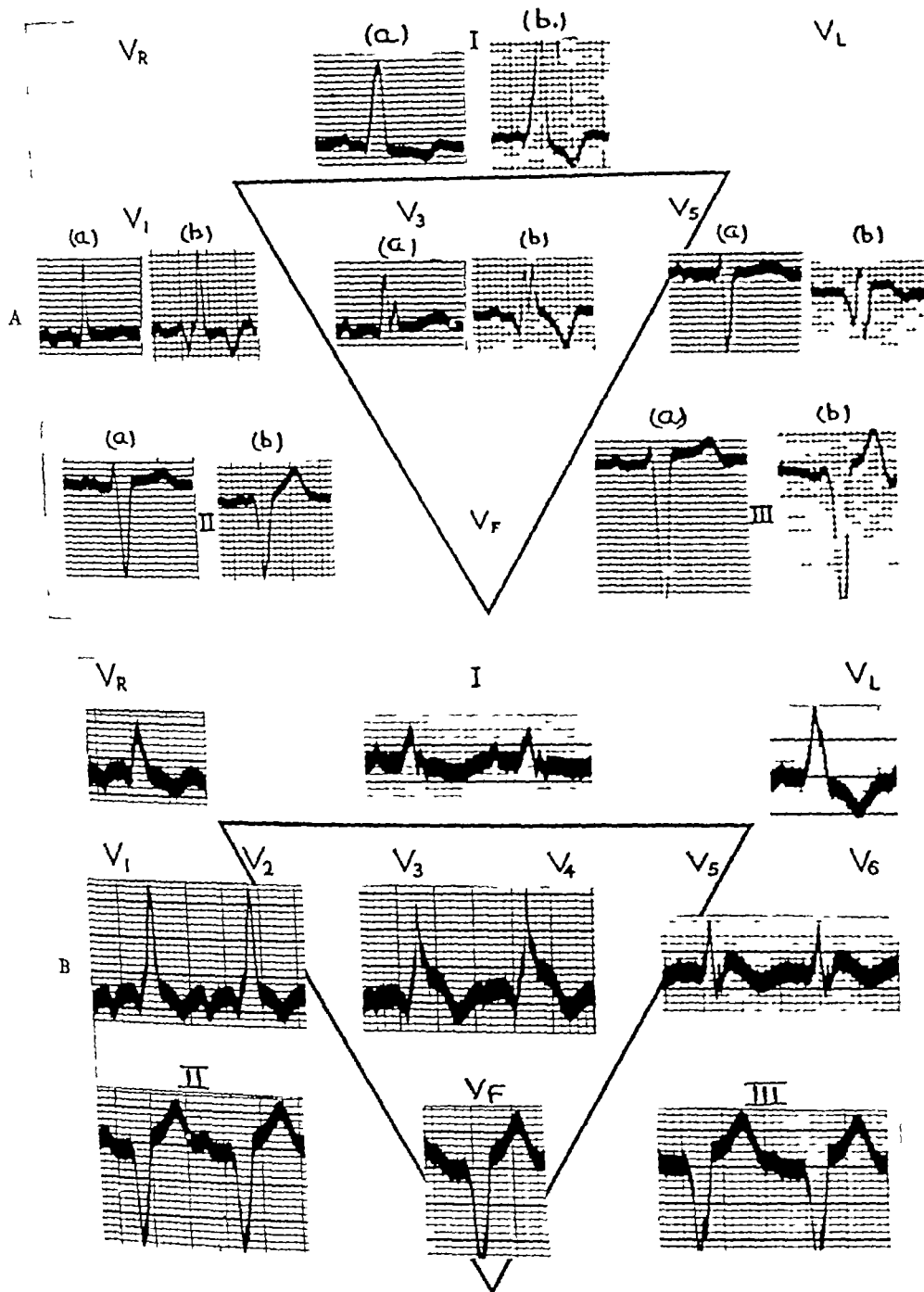
FIG 11—Anterior cardiac infarction and right bundle branch block   (A) The control graph (*a*) was taken on 9/9/46 and shows right bundle branch block with a vertical heart   The second curve (*b*) taken on 24/9/46 shows prominent Q waves and inverted T waves in all chest leads due to anterior cardiac infarction   (B) Anterior infarct (11 days old) shown in leads V1 and V3   The right bundle branch block complex in lead V1 is transmitted to lead VL and hence to standard lead I, the heart being electrically vertical   Standard limb leads thus resemble left bundle branch block
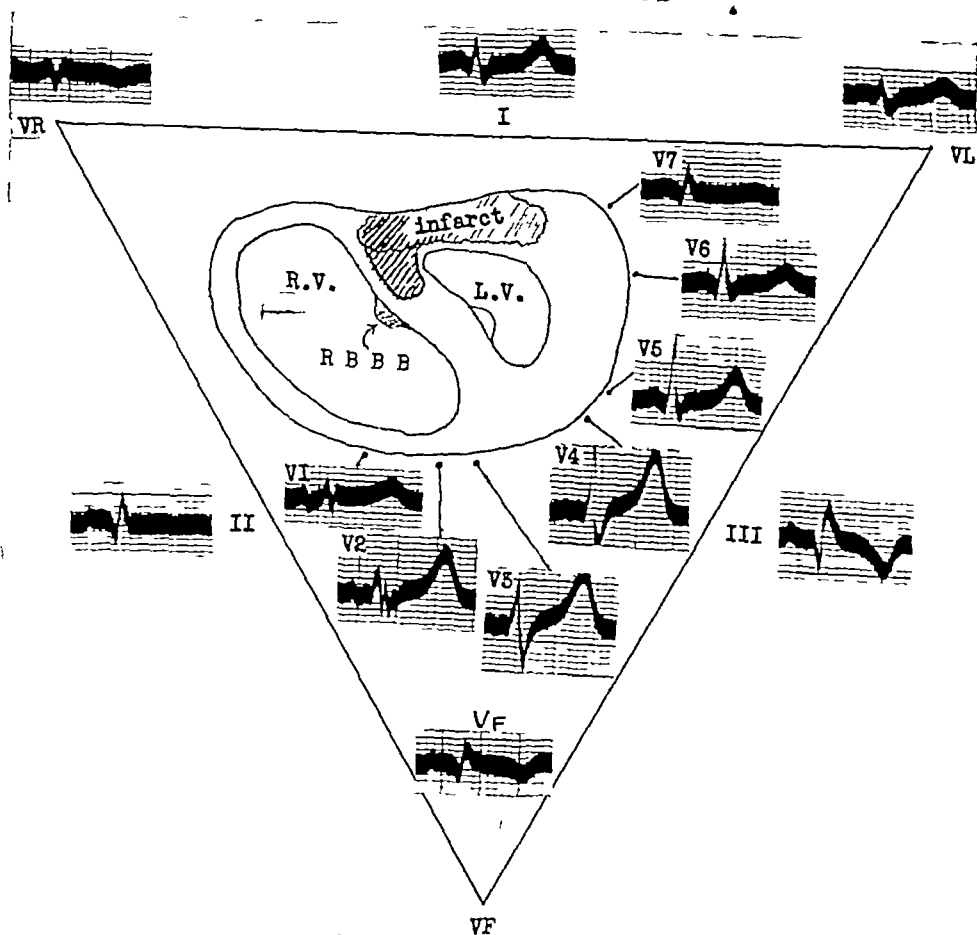
FIG 12 —Posterior cardiac infarction and right bundle branch block   Pathological Q waves are well seen in lead VF and in standard leads II and III

the septum is often, but not invariably, involved In a necropsy study of 30 cases of gross septal infarction, Master *et al* (1937) found that impaired intraventricular conduction had been present in only 12 cases

Attempts to correlate the site of coronary occlusion with the occurrence and type of bundle branch block have been reported frequently (White, 1934, Saphir *et al*, 1935, Applebaum and Nicholson, 1935, Barnes, 1935, Pratsicas, 1936, Fischer, 1938, Master *et al*, 1938) Applebaum and Nicholson concluded from their necropsy findings in 11 cases that it was impossible to determine which vessel was occluded by the type of block present, for there was usually severe and extensive involvement of the entire coronary system   Master and his co-workers (1938) also submitted that it was

impossible to locate the site of an infarct from the type of bundle branch block present   Reviewing their findings in 20 cases examined at necropsy these authors reported a similar incidence of conduction defects whether the left or right coronary artery was occluded   In 16 of their 20 cases however, the infarct did involve the septum   When the QRS interval exceeded 0 14 sec septal infarction was invariable

The apparent lack of correlation between the situation of coronary occlusion and cardiac infarction, on the one hand and bundle branch block on the other might be explained by the presence of a gradually developed collateral circulation in the areas supplied by vessels showing long standing occlusion (Blumgart and Schlesinger 1940)

There were 11 necropsies in the present series
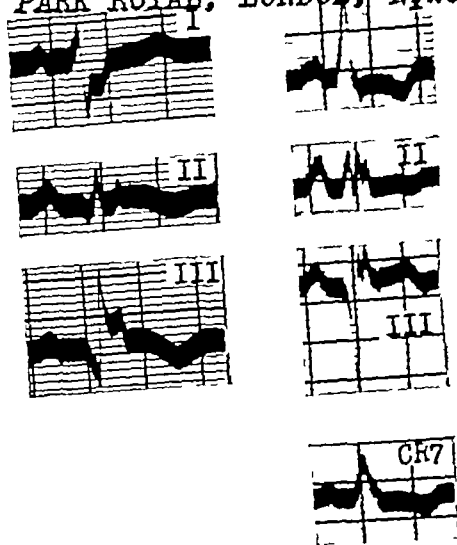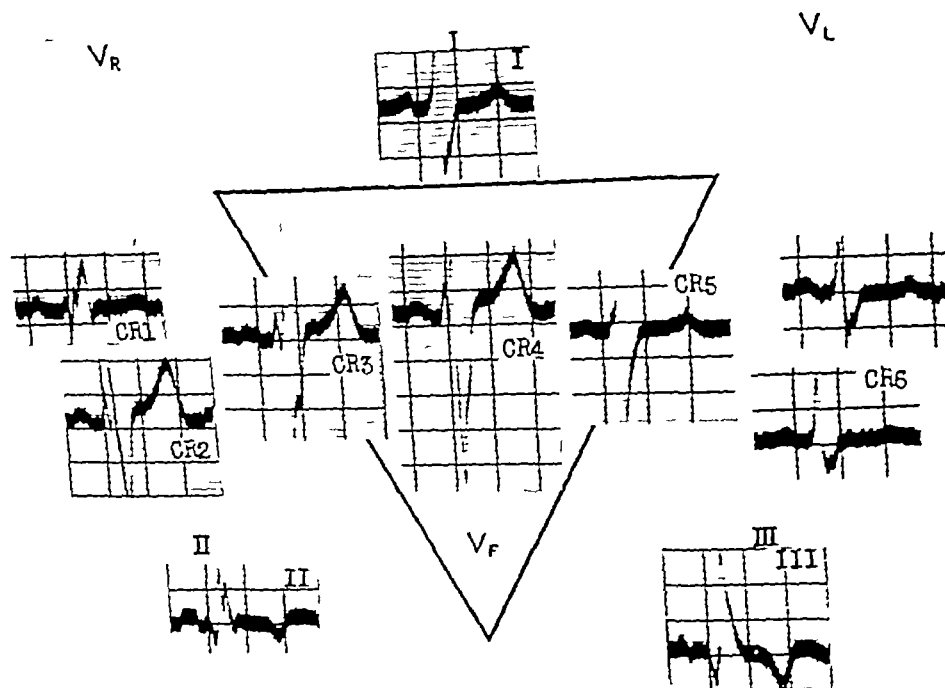
FIG 13 —(A) 9/7/45 showing right bundle branch block and posterior infarction (B) 11/10/47, showing left bundle branch block after fresh posterior infarction (C) Posterior cardiac infarction and right bundle branch block The infarction is shown well in standard leads but not in lead CR7

Z
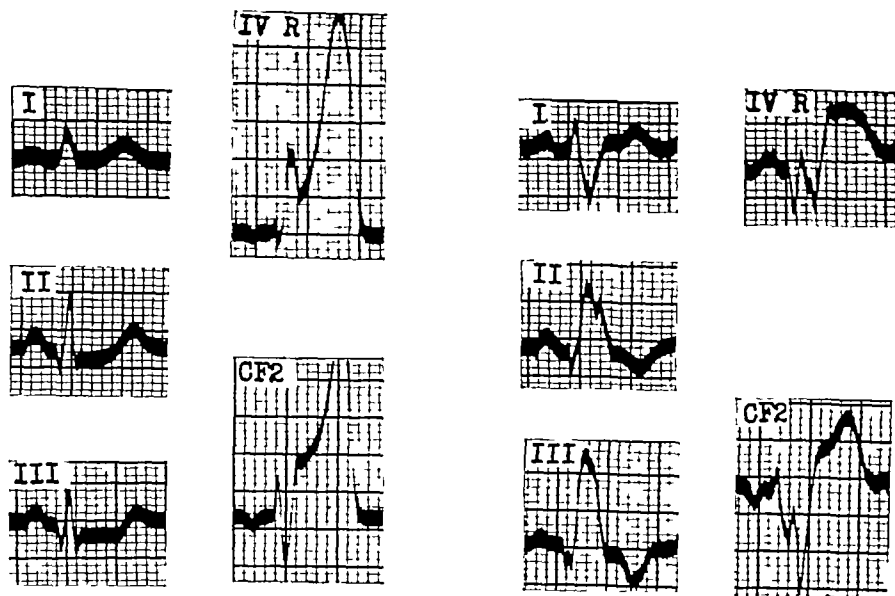
FIG 14 —Anterior and posterior infarction associated with left bundle branch block in a vertical heart   (A) Normal conduction 6 hours after the onset   Lead 4R shows elevation of the R–T segment and an enormous T wave indicating an anterior infarct a few hours old   The Q wave in leads II and III is derived from lead VF (not shown) to which left ventricular surface potentials are transmitted   (B) 5 days later   Left bundle branch block has developed as shown by lead CF2   The heart being vertical standard leads resemble right bundle branch block   Changes of acute anterior infarction are shown in lead IVR   Necropsy showed both anterior and posterior infarction

The main findings, summarized in Table VII, confirm the absence of any clear relationship between the vessel occluded, the bundle branch predominantly involved, and the situation of the infarct

In 9 cases, however, the infarct involved the ventricular septum   In the 2 instances in which the septum escaped the infarct was situated in the posterior wall of the left ventricle   the electrocardiogram showed left bundle branch block in one (Case 75) and right bundle branch block in the other (Case 76)   In 4 of the 9 cases in which the ventricular septum was infarcted, the QRS interval equalled or exceeded 0 14 second

In a control study we found septal involvement in 58 of 100 unselected cases of cardiac infarction examined at necropsy   From the figures discussed above it is clear that the septum is involved more frequently (80 per cent) when there is bundle branch block   If pathological Q waves occurred in all cases of cardiac infarction, left bundle branch block would not therefore be expected to obscure the pattern in 80 per cent of cases   The actual figure of 48 per cent found in our analysis more or less harmonizes with these expectations for a minority of infarcts are too shallow to cause Q waves

SUMMARY AND CONCLUSIONS

Sixty cases with a history or other evidence of cardiac infarction and an electrocardiogram showing bundle branch block have been collected and analysed in order to determine the frequency with which the cardiographic signs of cardiac infarction occur with bundle branch block

The series comprised 33 examples of left and 27 of right bundle branch block   Cardiographic signs of cardiac infarction were present in 41 cases (68 per cent)

These signs were found in 48 per cent of the cases with left bundle branch block   and in 93 per cent of those with right bundle branch block   As a corollary it should be stressed that the signs of infarction were suppressed in approximately half the cases complicated by left bundle branch block

The belief that significant Q waves in left ventricular surface leads in cases with left bundle branch block denote septal infarction is supported by limited necropsy evidence

In the presence of left bundle branch block the signs of anterior infarction were revealed as frequently with standard limb leads as with multiple

chest leads and unipolar limb leads In the presence of right bundle branch block, signs of anterior infarction were sometimes seen only in the chest leads

The signs of posterior infarction were practically confined to the standard limb leads and to lead VF whether the block was in the left or right bundle branch

TABLE VII

NECROPSY FINDINGS IN ELEVEN CASES OF CARDIAC INFARCTION AND BUNDLE BRANCH BLOCK

Case No	Electrocardiogram			Necropsy
	QRS (sec)	Block	Infarct	
1	0 14	Left	Anterior	*Arteries* Generalized severe atheroma No thrombosis discovered *Infarct* Recent infarction of anterior wall of left ventricle and upper three-quarters of ventricular septum Fibrosis involving these areas
8	0 12	Left	Anterior	*Arteries* Slight atheroma of main vessels Smaller sub divisions showed diffuse widespread atheroma No occlusion *Infarct* Anterior wall of left ventricle and ventricular septum Diffuse fibrosis involving left ventricle and ventricular septum
10	0 12	Left	Anterior	*Arteries* Calcified atheroma marked in main arteries Left anterior descending branch and right coronary completely occluded by organized thrombus The left circumflex partially occluded by calcified atheroma *Infarct* Extensive old infarction of anterior and posterior walls of left ventricle and ventricular septum Recent infarction involving anterior wall and ventricular septum Widespread subendocardial fibrosis of left ventricle
20	0 12	Right	Anterior	*Arteries* Both right and left coronaries completely occluded and calcified for a distance of 1–2 cm commencing 2 cm beyond their origin *Infarct* Extensive recent infarction involving postero-inferior two-thirds of ventricular septum, apex and lower one third of anterior wall of left ventricle Whole thickness of anterior wall partially necrotic Old infarction in posterior wall of left ventricle
21	0 12	Right	Anterior	*Arteries* Left anterior descending and right coronary arteries occluded *Infarct* Recent extensive infarction involving anterior wall of left ventricle and ventricular septum Old infarction of posterior wall of left ventricle
23	0 16	Right	Anterior	*Arteries* Generalized atheroma Anterior descending branch of left coronary thrombosed in proximal 3 cm, distal part was laminated and calcified and proximal part fresh and homogeneous *Infarct* Apex of left ventricle and lower part of ventricular septum recently infarcted.
28	0 16	Right	Anterior	*Arteries* Anterior descending branch of left coronary occluded in proximal 2 cm Left main coronary and circumflex branch normal Moderate atheroma of right coronary *Infarct* Recent infarction of anterior wall of left ventricle and of ventricular septum
30	0 12	Right	Anterior	*Infarct* Recent extensive infarction of anterior wall of left ventricle and of ventricular septum Old fibrosed infarction of posterior wall of left ventricle
49	0 16	Right	Anterior and Posterior	*Infarct* Recent infarction of apex and anterior and posterior walls of left ventricle and of ventricular septum
75	0 12	Left	—	*Arteries* Marked atheroma of entire coronary tree Thrombosis of circumflex branch of left coronary *Infarct* Large area of posterior wall of left ventricle recently infarcted
76	0 12	Right	—	*Infarct* Thinning and fibrosis of old infarction involving posterior wall of left ventricle

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AORTIC SINUS ANEURYSMS

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The three slight dilatations of the aorta immediately above the corresponding valve cusps, known as the aortic sinuses of Valsalva, are almost entirely intracardiac and lie near important parts of the heart (Fig. 1) Aneurysms arising from these sinuses may extend into the cardiac chambers and encroach upon the pulmonary valve, the atrioventricular valves, the conducting bundle, or the pulmonary or coronary arteries, or may lead to aortic regurgitation by deforming the aortic ring They may rupture into one of the cardiac chambers, the pulmonary artery, or the pericardium, and sometimes communicate from birth with a cardiac chamber or the pulmonary artery To these various complications such aneurysms owe much of their interest

Aneurysms confined to the aortic sinuses are uncommon, Smith (1914) noted that in 8138 necropsies only 7 were found and, in all, only 20 cases were confirmed at necropsy prior to 1914 These aneurysms may be due to any of the usual causes, but those of congenital origin are of particular interest The first recorded case of this type appears to be that of Thurnam (1840) and when Abbott (1936) collected her 1000 cases of congenital heart disease she was able to find only 12 congenital aortic sinus aneurysms recorded (Bauer & Astbury, 1944)

Our objects in this paper are to describe four new cases, which present certain features of interest, and to review the available clinical and pathological material particularly so far as it illustrates the pathological differences between the acquired and congenital types of aneurysm or aids the clinical diagnosis of congenital aneurysms Some preliminary discussion of the nomenclature of the aortic sinuses and of the topography of the aortic root is desirable to clarify the anatomical features of the cases to be described

NOMENCLATURE OF THE AORTIC SINUSES

The many ways of naming the aortic cusps and their sinuses are so confusing that it is often difficult to identify the sinus described In Table I we have enumerated five methods of nomenclature and in Fig 2 have indicated the sinus to which each name refers The standard nomenclatures [Old Terminology Basle Anatomical Nomenclature 1895 (B N A), Birmingham Revision, 1933 (B R)] have assumed that one aortic sinus lies anterior and two posterior and always placed in an anterior position the sinus from which the right coronary artery arises, but Walmsley (1929) has pointed out that sometimes two aortic sinuses lie anterior, and one posterior (Fig 2), he suggested that sinuses related to the coronary arteries should be named right and left coronary sinuses, the third sinus being called the non-coronary sinus This nomenclature is easy to understand and allows the sinuses to be named when the heart has been removed from the body and the sinuses exposed by opening the aorta, we have therefore adopted it in this paper

TOPOGRAPHY OF THE AORTIC ROOT

The structures adjacent to the aortic sinuses are of considerable importance in discussing the clinical and pathological features of sinus aneurysms, these structures are illustrated in Fig 1 and described in the caption

The annulus fibrosus Between the aorta proper and the main body of the left ventricle there is a tubular zone of fibrous tissue, the annulus fibrosus, which forms an important part of the wall of the aortic sinuses and extends downward to become incorporated in the aortic vestibule of the left ventricle It is believed that congenital sinus aneurysms arise from defective development of the bulbar septum which divides the primitive exit
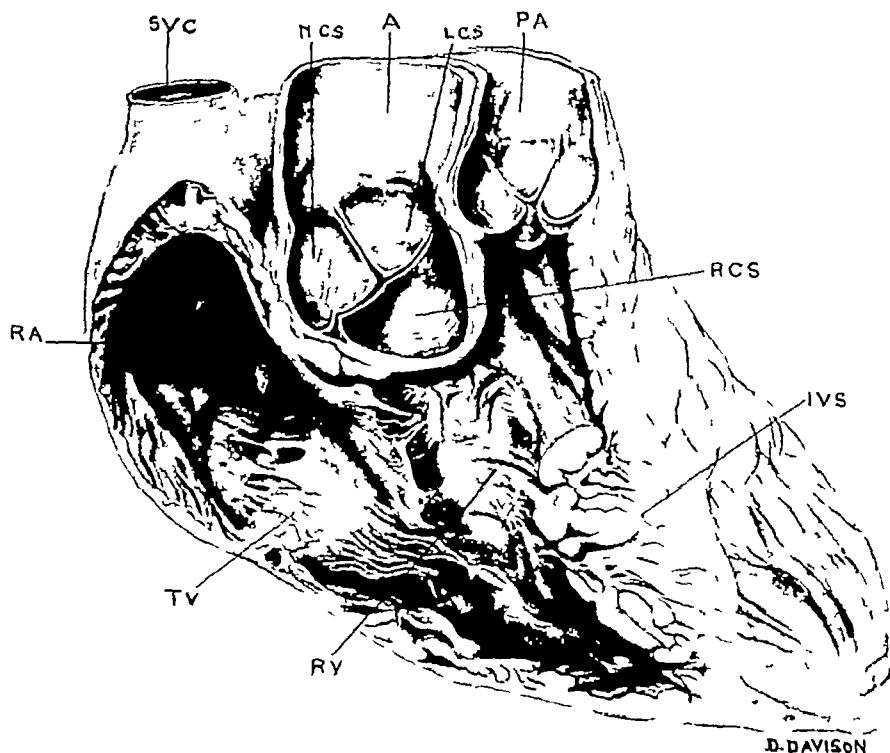
FIG 1 —*Position of the aortic sinuses* From a normal heart, fixed unopened, with vessels and cham bers distended The anterior and part of the right walls of the right ventricle and right auricle have been removed and the aorta opened The anterior part of the ventricular septum (I V S) has been sectioned The right coronary sinus (R C S) projects into the conus of the right ventricle (R V) The non-coronary sinus (N C S) projects into the right auricle (R A) and the tricuspid valve lies below adjacent sectors of the non-coronary and right coronary sinuses The left coronary sinus (L C S) with its coronary artery can be seen postero-laterally It is related behind to the mitral valve and the left auricle S V C—Superior vena cava A —Aorta P A —Pul monary artery

tube of the heart, the bulbus cordis, into right and left halves Since the annulus fibrosus arises from the bulbus cordis and forms part of the wall of the aortic sinuses, it is a particularly important structure to study when a sinus aneurysm is present

CASE REPORTS

Case 1 A congenital aneurysm of the right coronary sinus associated with a bulbar ventricular septal defect, clinically simulating patency of the ductus arteriosus and complicated by subacute bacterial endocarditis

In April, 1939, a schoolboy age 12, was referred to Dr Crighton Bramwell on account of a heart murmur first discovered during a respiratory infection in infancy Apart from tonsillitis when 5, he had enjoyed good health At school he led a normal life and played games, including football, without cyanosis or unusual dyspnœa At 10 years of age tonsillectomy was advised, but not performed owing to the cardiac murmur He suffered from epistaxis on several occasions and in August and December, 1938 severe attacks occurred

On examination his general development was normal, height 60 inches, weight 80 lb His exercise tolerance was good and there was no cyanosis or finger clubbing The pulse was regular, rate 80, the blood pressure 125/40 To the left of the sternum, at the base, systolic and diastolic murmurs were heard Cardioscopy showed considerable enlargement of both ventricles, but a cardiogram was normal apart from R waves of

TABLE I

NOMENCLATURE OF THE AORTIC SINUSES

	Walmsley (1929)	Common position		Less common position	
	(a)	(b) B R 1933	(c) B N A 1895	(d)	(e)
1	Right coronary	Anterior	Anterior	Right	Right anterior
2	Non-coronary	Right	Right posterior	Posterior	Posterior
3	Left coronary	Left	Left posterior	Left	Left anterior

exceptionally high voltage in the standard limb leads The condition was diagnosed as patency of the ductus arteriosus

In January, 1942, subacute bacterial endocarditis was suspected and he was admitted to hospital Seven weeks prior to admission he had a pyrexial illness lasting a few days accompanied by vomiting and shivering Subsequently his appetite failed to return and he complained of transient pains in the limbs, felt continually tired, lost weight, and was troubled by nocturnal sweating For a week before admission he suffered from substernal pain which frequently awakened him at night

On examination he weighed only 84 lb and was pale His temperature was 100 2° F Striking arterial pulsation was visible in the neck, the pulse was regular, rate 120, the blood pressure 120/30 A systolic thrill was palpable in the second and third left interspaces near the sternum accompanied by a harsh systolic murmur and a softer diastolic murmur, both maximal in the same position, but audible over the whole præcordium A teleradiogram showed considerable cardiac enlargement (cardiothoracic

ratio 0 66) involving both ventricles The cardiogram was similar to the previous record The liver was palpable two inches below the costal margin, there was no œdema but a few moist sounds were heard at the lung bases The spleen was palpable and there were scattered petechiæ on the abdomen chest, neck, and arms An Osler s node was found on the tip of the right little finger Blood culture yielded a growth of *Streptococcus viridans* His condition steadily deteriorated and three weeks after admission he collapsed suddenly and died the following day

At *necropsy* a few petechiæ were found on the arms, there was subcutaneous œdema of the trunk and effusions were present in the pericardial pleural, and abdominal cavities There was generalized passive congestion and infarcts were present in the spleen and right lung, these appearances were confirmed histologically

The *heart* was globular in shape and weighed 600 g The right atrium was slightly hypertrophied but the left was normal The right ventricle was slightly, and the left ventricle considerably hyper-
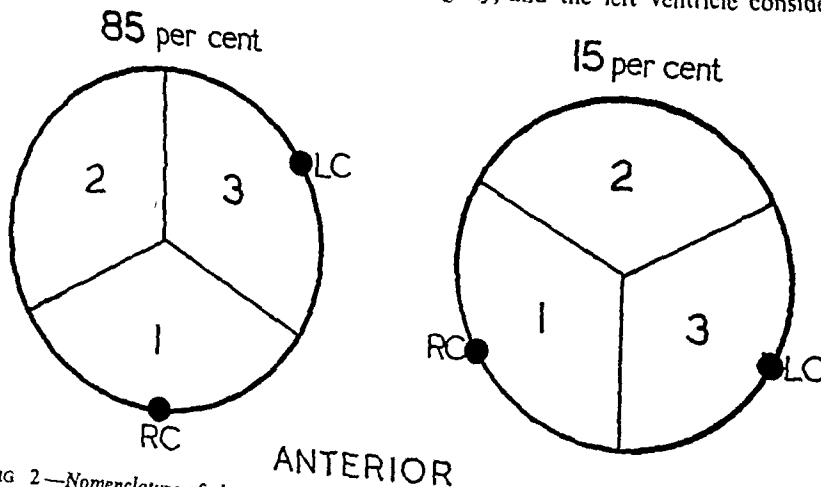
FIG 2—*Nomenclature of the aortic sinuses* (1), (2), and (3) are the sinuses named in Table I R C —right coronary artery L C —left coronary artery The percentages refer to Walmsley s (1929) estimate of the relative frequency of the two arrangements

trophied   The foramen ovale and the ductus arteriosus were closed   In the anterior part of the ventricular septum, immediately below the right coronary cusp, there was a triangular opening, base 1 3 cm , height 0 8 cm , communicating between the conus of the right ventricle and the aortic vestibule of the left ventricle (Fig 3)   This opening lay anterior to the membranous septum and above the septal and parietal muscle bundles, it was therefore a defect of the true bulbar septum   Vegetations characteristic of subacute bacterial endocarditis were present around the margins of the septal defect

The right coronary sinus was enlarged to form an aneurysm with a mouth 2 by 2 cm and a depth of 2 5 cm   From the upper limit of the mouth the wall of the aneurysm extended horizontally for a distance of 0 6 cm , and then curved downwards obliquely for 0 5 cm to a well defined transverse ridge   Below this the outer wall of the aneurysm was related to the muscle of the right ventricle and then joined the right coronary cusp   The size of the right coronary cusp was about normal but owing to the aneurysm, the intercommissural distance was small   consequently the cusp sagged downwards through the septal defect (Fig 3A), its lower part forming the upper margin of the communication between the ventricles   This sagging
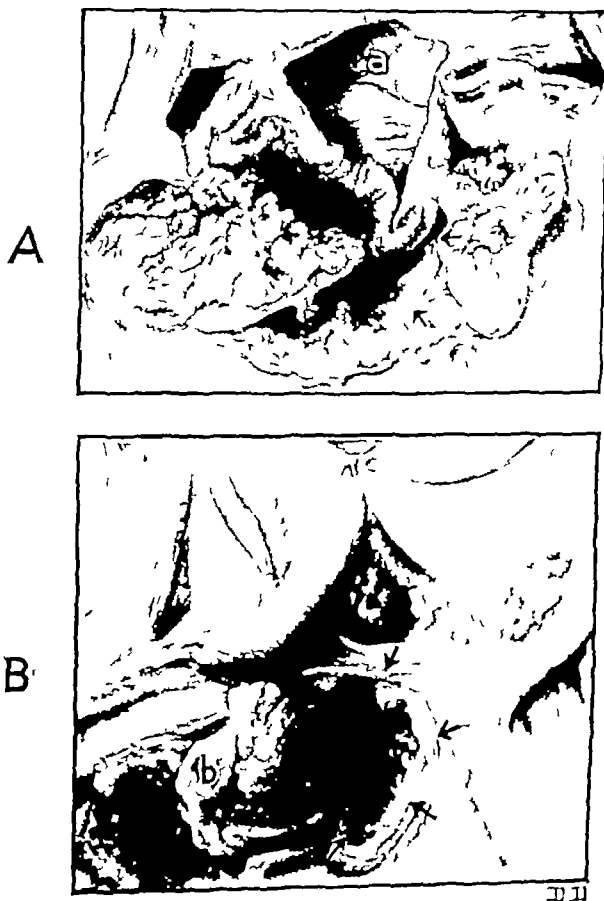
FIG 3 —*Case* 1   *From a drawing of the aneurysm   (A) Aortic and left ventricular aspect*
(a)—The aneurysm   The sagging of the right coronary cusp can be seen   The arrows indicate the margins of the ventricular septal defect, which is surrounded by the vegetations of bacterial endocarditis   *(B) Pulmonary and right ventricular aspect   (b)* The apex of the aneurysm projecting into the right ventricle through the septal defect   The margins of the septal defect are indicated by arrows

had made apposition of the aortic cusps impossible so that the valve was incompetent

The non-coronary aortic cusp was enlarged, measuring 3 cm between the commissures and the corresponding sinus was deeper than usual (1 9 cm) The left coronary cusp measured 1 5 cm between the commissures The right coronary artery was much smaller than the left, its orifice lying in the part of the aneurysm adjacent to the non-coronary sinus The left coronary orifice was puckered and lay near the commissure between its sinus and the non-coronary sinus

On *histological examination* the aorta and aortic valve cusps were normal apart from the vegetations and the inflammatory changes of bacterial endocarditis From the annulus fibrosus a tongue of fibrous tissue ran upwards to the transverse ridge on the aneurysm wall, lying between the muscle of the right ventricle and the endothelial lining of the aneurysm The aortic media terminated at the transverse ridge

In addition to the aneurysm, several congenital anomalies were present, a bulbar septal defect, an abnormal tongue of fibrous tissue arising from the annulus, and grossly unequal aortic cusps The aortic wall was free from disease other than bacterial endocarditis, which might have arisen upon the developmental defects In view of these findings, it seems justifiable to attribute the aneurysm to a developmental anomaly

The presence of aortic incompetence accounted for the collapsing pulse, the large pulse pressure and the diastolic component of the murmur The systolic component and the thrill were explicable by the presence of the ventricular septal defect

Case 2   A congenital aneurysm of the right coronary sinus, which ruptured into the conus of the right ventricle and led to progressive heart failure

In January, 1944, a man of 41, a chauffeur, was admitted to hospital, complaining of breathlessness and swelling of the legs and abdomen Heart disease was first found at the age of 24 when he had a severe attack of breathlessness and præcordial pain From that time he suffered from dyspnœa on exertion and præcordial pain Some weeks before admission he noticed swelling of the legs and abdomen and his dyspnœa became more severe He had never had rheumatic fever nor chorea and cyanosis had not occurred in childhood

On examination he was cyanosed, dyspnœic at rest and the neck veins were engorged The pulse was regular, rate 104 a minute, systolic blood pressure 140 mm diastolic end point uncertain, the sounds being audible to complete decompression The heart was enlarged, and a coarse systolic thrill was palpable over the whole præcordium most intense in the third left interspace near the sternum Very loud, coarse, systolic and diastolic murmurs of machinery type were audible over the whole præcordium, but best heard in the third left interspace near the sternum The liver was enlarged and tender and free fluid was present in the abdomen There was considerable œdema of the legs and sacral area

A cardiogram showed left axis deviation with depression of the RS–T segments in leads I and II these appearances were attributed to left ventricular enlargement A teleradiogram revealed considerable cardiac enlargement (cardio thoracic ratio 0 63) involving both ventricles but principally the left The pulmonary artery and the pulmonary vascular markings were prominent

With treatment by rest mercurial diuretics and digitalis he gradually improved but his œdema did not entirely disappear During his fourth week in hospital his condition began to deteriorate his œdema increased he became very breathless and was soon jaundiced and pyrexial he died after four weeks in hospital

Necropsy was performed by Dr G Stewart Smith The skin and mucous membranes were jaundiced and there was some œdema of the legs The whole upper lobe of the right lung was consolidated and typical of the stage of grey hepatization of lobar pneumonia Both lungs were congested and œdematous There was generalized chronic venous congestion

The *heart*, which we examined, weighed 640 g In the left half of the right coronary sinus there was a round opening 0 7 cm in diameter with rounded slightly irregular margins (Fig 4B) This led to a globular thin-walled cavity (Fig 4A), 2 cm in diameter, which projected into the conus of the right ventricle between the septal (posterior) and right anterior cusps of the pulmonary valve (Fig 4A) On the upper surface of the aneurysmal sac was an aperture approximately rectangular in shape 0 8 cm by 0 6 cm , with smooth, rounded and thickened edges The irregular shape of this opening suggested that it was due to rupture of the aneurysm and, since the edges were smooth and rounded, healing had occurred The aneurysm thus formed a communication between the aorta and the right ventricle The right coronary artery arose near the commissure between its sinus and the non-coronary sinus (Fig 4B)

In the outflow tract of the left ventricle, 0 5 cm below the aortic valve, was a fibrous band, lying on the interventricular septum, and extending from the right upper margin to the left upper margin of the anterior curtain of the mitral valve (Fig 4B)

FIG 4 —Case 2   From a drawing of the heart   (A) Pulmonary and right ventricular aspect   The perforated
globular aneurysm lies in the conus of the right ventricle just below the septal (posterior) and right
anterior cusps of the pulmonary valve   (B) Aortic and left ventricular aspect   (a) The opening of the
aneurysm in the right coronary sinus   The right coronary artery arises near the commissure between
its sinus and the non-coronary sinus

This abnormality occurred at about the level at which sub-aortic stenosis develops The wall of the left ventricle was slightly thickened (1 5 cm) and its cavity was dilated, this had led to the displacement of the ventricular septum towards the right ventricle The wall of the right ventricle was about twice the normal thickness (0 9 cm) and the columnæ carnæ and chordæ tendineæ were hypertrophied The conus of the right ventricle was considerably dilated but its body appeared only slightly dilated, though this was difficult to estimate owing to the displacement of the ventricular septum The circumference of the pulmonary valve measured 8 cm , the septal cusp was fenestrated The circumference of the aortic valve was 6 8 cm , and the left coronary cusp was slightly fenestrated The mitral valve measured 7 5 cm in circumference and the tricuspid valve 13 cm , both valves appeared normal

The absence of acquired heart disease and the presence of a congenital sub-aortic band of fibrous tissue make it reasonable to suppose that this aortic sinus aneurysm was of congenital origin While unruptured it is unlikely to have given rise to symptoms, and it seems probable that the onset of symptoms 17 years before death coincided with rupture into the right ventricle, the healing of the margins of the rupture is consistent with this opinion

Case 3 A dissecting aneurysm of the right coronary sinus communicating with the right and left ventricles and leading to an intracardiac hæmatoma around the right coronary artery

In March, 1941, a married woman of 54 was admitted to hospital, complaining of vomiting and palpitation Her previous health had been good except for an attack of rheumatic fever at age 27, when she was confined to bed for a year, she was subsequently told that she had a " weak heart " At 50, she noticed breathlessness on exertion and began to suffer from attacks of palpitation of sudden onset and offset, lasting 20 to 30 minutes In June, 1940, she noticed increasing thirst, polyuria, and progressive weakness, a diagnosis of diabetes mellitus was made She remained fairly well until two weeks before admission when she lost her appetite and became easily tired, for 48 hours before admission she vomited repeatedly and became drowsy On the evening before admission she had an attack of palpitation which lasted several hours, during the night she awoke owing to a recurrence of the palpitation which continued until admission

On *examination* it was found that the heart was completely irregular at a rate of 172 a minute Blood pressure 120/85 The cervical veins were

engorged and moist sounds were present at both lung bases The temperature was 100° F and the urine contained a considerable quantity of sugar and acetone, blood sugar 355 mg per 100 ml The condition was diagnosed as diabetes mellitus with hyperglycæmic pre-coma, and uncontrolled auricular fibrillation

She was treated with insulin, glucose, and intravenous digoxin followed by digitalis by mouth Her heart rate fell to 94 in 24 hours, when an apical diastolic murmur, typical of mitral stenosis, became audible A cardiogram confirmed the presence of auricular fibrillation A teleradiogram of the chest showed slight cardiac enlargement The diabetic ketosis was rapidly controlled, but her temperature remained raised owing to a *B coli* pyelitis which was treated by sulphapyridine After three weeks she was allowed up for a short time, a week later she had an attack of paroxysmal nocturnal dyspnœa She was confined to bed and the attacks ceased after four nights Four days later she suddenly collapsed, complaining of tightness across the chest, she became cyanosed and died within a few minutes

At *necropsy* effusions were present in both pleural cavities and there was generalized chronic venous congestion The *heart* weighed 480 g , the left ventricle was hypertrophied but the right appeared normal except where the aneurysm projected into it Both atria appeared normal The mitral valve was moderately stenosed, the aortic cusps were thickened but the pulmonary and tricuspid valves appeared healthy There was slight atheroma of the coronary arteries, especially near the orifice of the right coronary

The lower part of the right coronary sinus formed an aneurysm about 3 cm deep extending towards, and projecting into, the conus of the right ventricle (Fig 5) The upper part of the inner (aortic) wall of the aneurysm was formed by the right coronary cusp, the middle part of the wall was disorganized and interrupted by a perforation communicating with the left ventricle, the lowest part of the inner wall was formed by the upper part of the ventricular septum The apex of the aneurysm projected into the right ventricle The outer wall was formed by a large, grey, necrotic mass, 6 by 4 cm , which enclosed the first part of the right coronary artery The upper part of this mass contained a recent hæmorrhage The greater part of the aneurysm was lined by loose blood clot, when this was removed a smooth lining of adherent thrombus was seen

Histology Normally the annulus fibrosus is of triangular shape and covered by a thin layer of elastic tissue on its aortic and left ventricular surfaces (Fig 6A), the aortic layer is continuous with

FIG 5 —*Case* 3   *From a drawing of the heart*   (*a*)
Aorta   (*b*) Aneurysm   (*c*) Hæmatoma

the internal elastic tissue of the aorta and the ventricular layer joins the subendothelial elastic tissue on the left side of the ventricular septum and is continuous with the subendothelial elastic tissue of the right ventricle   In the specimen the annulus fibrosus had become separated from the aortic media   The left ventricular layer of elastic tissue of the annulus could be traced through to the elastic tissue on the left side of the membranous septum   At the apex of the aneurysm the distribution of elastic tissue strongly suggests that this was the reflected right side of the septum (Fig 6C)

These observations are explicable if the aneurysm had been formed as suggested in Fig 6   First, blood penetrated between the termination of the aortic media and the annulus fibrosus (Fig

6B)   then it spread into the subpericardial fat to form the large hæmatoma   It next separated the muscle of the right ventricle from the annulus and then extended in three directions, (1) to rupture through the endothelium of the right ventricle (2) to split the membranous septum and reflect it with its elastic layer towards the right ventricle and (3) to sever the apex of the annulus from the septum and to rupture through the endothelium of the left ventricle (Fig 6C)   Thus the dissection lay between the annulus and the muscle of the right ventricle and had communicated with both ventricles

Although there is little doubt that this was a dissecting aneurysm arising in the right coronary sinus at the junction of the aortic media with the annulus fibrosus, it is more difficult to decide the nature of the lesion that led to the dissection Examination of the aorta showed none of the degenerative changes such as cystic medial necrosis often found in dissecting aneurysms   There were however, inflammatory changes with a round cell reaction, fibroblasts, and new capillaries These changes were sometimes perivascular but unlike the changes of syphilis, they were confined to the adventitia and did not invade the media Although the inflammatory changes were most severe and acute at the point of rupture, they were also present in the whole of the intrapericardiac aorta   There were also striking histological changes in the aortic and mitral valve cusps, which were scarred and vascularized by thin walled blood vessels and in the myocardium small areas of perivascular fibrosis were found   In the pericardium there were recent inflammatory changes with some cellular foci which resembled Aschoff bodies though giant cells were not found   The association of these changes in the valves and myocardium with mitral stenosis confirms their rheumatic origin and suggests that the recent inflammatory changes in the pericardium and aorta were due to a recrudescence of cardiovascular rheumatism   The close resemblance of the aortic lesions to those described as rheumatic aortitis by Pappenheimer and von Glahn (1924) strengthens this hypothesis   It is therefore probable that the dissection arose owing to the development of active aortitis possibly rheumatic in origin

Case 4   *An aneurysm of the non coronary aortic sinus projecting into both atria probably due to bacterial endocarditis*

A married woman aged 52 was first seen in June 1942 on account of hæmatemesis due to a gastric ulcer   At this time a soft apical systolic murmur was noticed but no signs of organic heart disease blood pressure 135/85   Hæmatemesis recurred in
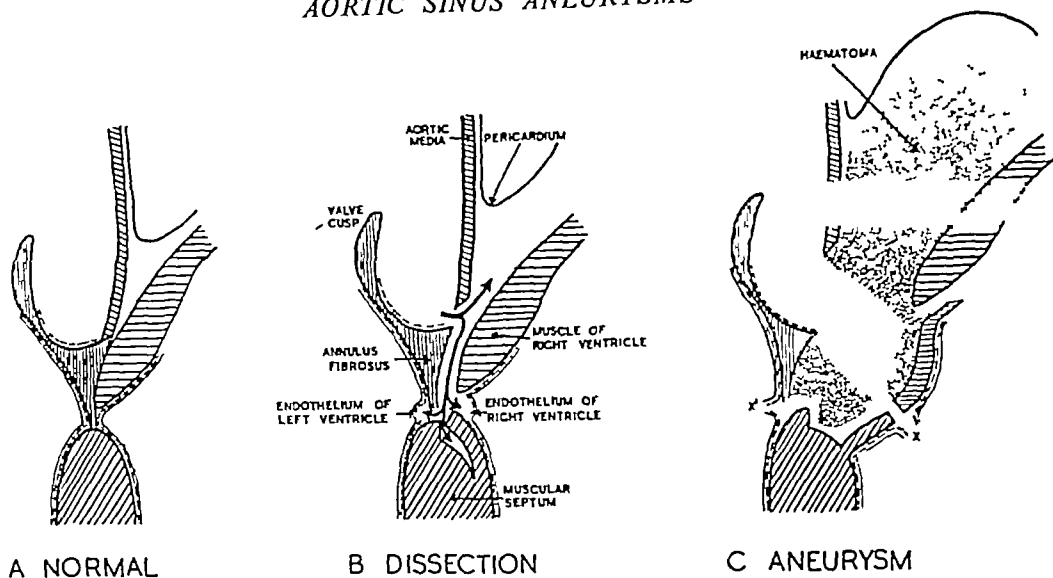
FIG 6 —*Case* 3 *The formation of the aneurysm* (*A*) *Normal structure of aortic root in section through right coronary sinus* The distribution of elastic tissue is shown by interrupted lines The structures are named in (*B*) (*B*) *Mode of dissection* The annulus fibrosus has been separated from the termination of the aortic media, the subsequent directions of dissection are indicated by arrows (*C*) *Aneurysm* By comparison with (*B*) the way in which the aneurysm has formed can be seen

June, 1943, and again in September, 1945, when she was re admitted to hospital

Examination Blood pressure 140/90 mm Apical systolic murmur still present Hæmoglobin 74, falling to 64 per cent in a few days Radioscopy showed the heart at the upper normal limit of size Slight fever was present and persisted White cell count 5800–7200 per c mm Gallstones were demonstrated by cholecystogram Eleven septic teeth were extracted without any improvement in her condition On January 4, 1946, she had a sudden gripping mid-sternal pain lasting twelve hours and became breathless A systolic thrill and murmur then appeared in the 2nd left interspace near the sternum, and a high-pitched diastolic murmur along the left sternal border The pulse became collapsing, blood pressure 145/55 mm A diagnosis of ruptured aortic cusp due to infective endocarditis was made, and blood culture showed a non hæmolytic, penicillin-sensitive streptococcus In spite of apparent control of the infection with penicillin, she died from heart failure three weeks later

At *necropsy* bilateral pleural effusion, general passive congestion splenic and renal infarcts, and chronic gastritis were found The *heart* weighed 470 g From the non-coronary sinus an aneurysm, 2 5 cm in diameter, projected backwards into the atria (Fig 7 and 8) The interatrial septum ran across the aneurysm dividing it into two unequal parts, one third lying in the right atrium and two-thirds in tne left The non-coronary cusp was thickened and calcified and, in the portion lying above the mitral valve, there was a perforation 1 7 cm in diameter, surrounded by small crumbling vegetations The other two aortic cusps were thickened and the commissure between them was calcified Many small vegetations were present on the margins of all cusps No abnormality was found in any other valve The cavity of the left ventricle was moderately dilated and the ventricular wall slightly thickened The other chambers appeared normal Atheromatous changes were present in the coronary arteries but were not severe

Histology The wall of the aneurysm consisted of three layers, an outer layer of fibro-elastic tissue (the atrial endocardium), a middle layer of muscle, and a thick inner layer of fibrous tissue The inner and middle layers were separated by small islands of elastic tissue which could be traced from the wall of the aneurysm into the elastic layer of the aortic media Embedded in the inner layer were small areas of calcification The aneurysm was partly lined by organizing thrombus which was sometimes covered by a thin layer of fibrous tissue In the aortic adventitia adjacent to the aneurysm, there was a widespread, mainly polymorphonuclear, inflammatory reaction which had, at one point, spread into the aneurysm wall Newly formed fibrous tissue extended from this area to the inner wall of the aneurysm and into the vegetations on the

Fig 7 —*Case* 4 *From a drawing of the heart* (*A*) *Aortic and left ventricular aspect*
The arrow indicates the aneurysm across its mouth a strip of tissue represents the
remains of the non-coronary aortic cusp below this lies the large perforation of
the cusp (*B*) The remaining part of the anterior aortic cusp has been removed to
reveal the extent of the aneurysm The vegetations of bacterial endocarditis are
visible in (*A*) and (*B*)

AORTIC SINUS ANEURYSMS

FIG 8—Case 4 *From a drawing of the atrial aspect of the aneurysm* The atrial septum, which crosses the aneurysm has been cut The left atrium and the mitral valve (M) lie to the left of the cut edge, the right atrium and the tricuspid valve (T) to the right

non-coronary cusp The aortic media was entirely free from inflammatory changes The normal architecture of the non-coronary cusp was greatly distorted and much calcification was present The histology of the mitral valve was normal Sections from the ventricular septum showed a diffuse, fairly acute, myocarditis

The aneurysm might have developed owing to the bacterial endocarditis, or it could have been of congenital origin and the focus for the bacterial endocarditis It is not difficult to understand how the bacterial endocarditis could have led to this aneurysm for the position of the inflammatory reaction in the aorta was such that it might have caused a separation of the annulus fibrosus from the aortic media, thus exposing the muscle of the atria, which would be stretched by the intra-aortic pressure to form the aneurysm In another case of subacute bacterial endocarditis we have seen the first stage of this process, for the annulus fibrosus of the non-coronary aortic cusp had been separated from the aortic media by a gap of 2 mm , through this gap blood had penetrated to form a hæmatoma between the annulus fibrosus and the atrial muscle If this had occurred in the present case and the separation had extended to expose the atrial muscle, thrombosus would have occurred on the exposed

muscle surface and subsequent organization could have given rise to the fibrous lining of the aneurysm The mode of formation thus resembles that in Case 3, but there the dissection started in the right coronary sinus and blood leaked into the loose subpericardiac tissues forming a hæmatoma In the present case the leakage was limited by the close relationship of the non-coronary sinus to the atrial muscle, so a large hæmatoma could not form We believe this to be the probable explanation of the histological structure of the aneurysm wall, so we do not suggest a congenital origin in this case The absence of other congenital anomalies, which nearly always accompany congenital sinus aneurysms, supports this conclusion There was no proof of an old lesion of the aortic valve upon which the bacterial endocarditis could have arisen, but the valve was so greatly deformed by the infection that old rheumatic disease cannot be excluded

Cases 3 and 4 illustrate the difficulty that may be encountered in deciding the ætiology of sinus aneurysms, and emphasize the importance of adequate histological examination in these cases

DISCUSSION

Aneurysms of the aortic sinuses may be divided into two groups, acquired (so-called " spontan-

FIG 7—*Case* 4 *From a drawing of the heart* (*A*) *Aortic and left ventricular aspect* The arrow indicates the aneurysm across its mouth a strip of tissue represents the remains of the non-coronary aortic cusp below this lies the large perforation of the cusp (*B*) The remaining part of the anterior aortic cusp has been removed to reveal the extent of the aneurysm The vegetations of bacterial endocarditis are visible in (*A*) and (*B*)

AORTIC SINUS ANEURYSMS

FIG 8 —*Case* 4   *From a drawing of the atrial aspect of the aneurysm*   The atrial septum, which crosses the aneurysm, has been cut   The left atrium and the mitral valve (M) lie to the left of the cut edge, the right atrium and the tricuspid valve (T) to the right

non-coronary cusp   The aortic media was entirely free from inflammatory changes   The normal architecture of the non-coronary cusp was greatly distorted and much calcification was present   The histology of the mitral valve was normal   Sections from the ventricular septum showed a diffuse, fairly acute, myocarditis

The aneurysm might have developed owing to the bacterial endocarditis, or it could have been of congenital origin and the focus for the bacterial endocarditis   It is not difficult to understand how the bacterial endocarditis could have led to this aneurysm for the position of the inflammatory reaction in the aorta was such that it might have caused a separation of the annulus fibrosus from the aortic media, thus exposing the muscle of the atria, which would be stretched by the intra-aortic pressure to form the aneurysm   In another case of subacute bacterial endocarditis we have seen the first stage of this process, for the annulus fibrosus of the non-coronary aortic cusp had been separated from the aortic media by a gap of 2 mm , through this gap blood had penetrated to form a haematoma between the annulus fibrosus and the atrial muscle If this had occurred in the present case and the separation had extended to expose the atrial muscle, thrombosus would have occurred on the exposed

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Cases 3 and 4 illustrate the difficulty that may be encountered in deciding the aetiology of sinus aneurysms, and emphasize the importance of adequate histological examination in these cases

DISCUSSION

Aneurysms of the aortic sinuses may be divided into two groups, acquired (so-called " spontan-

eous ") aneurysms, which arise in a diseased aorta, and aneurysms due to developmental defects Since there appear to be important pathological, radiological, and clinical differences between the two types, which have not usually been described separately, we have considered it worthwhile to compare verified cases from both groups including our own cases and have collected 25 reported cases of congenital sinus aneurysms proved at necropsy, together with 22 acquired aneurysms *confined* to the aortic sinuses and confirmed pathologically We have not included acquired aneurysms reported prior to 1914 since these were often inadequately described and the ætiological importance of syphilis was not appreciated   The sources of these cases are given below

Congenital Aneurysms

R C S * Thurnam (1840), Beck (1842), *Rickards (1881)*, *Charteris (1883)*, Livingston (1883), Cayla (1885), Kryzwicki (1889), White (1892), Kraus (1902), Hart (1905) 3 cases, Eppinger (1916), Abbott (1919), Jacobi and Heinrich (1933), Hirschboeck (1942), King (1942), Macleod (1944), Our cases 1 and 2

N C S * Goehring (1920), Laederich and Pomeau-Delville (1928), Duras (1944), Kawasaki and Benenson (1946), Herson and Symons (1946)

Acquired Aneurysms

R C S * Smith (1914) Cases 1 and 2, Noack *(1919)*, *Scott (1924) Case 1*, Sheldon (1926), Abbott (1932), Benson, Hunter, and Manlove (1933) Case 1, Snyder and Hunter (1934) Case 2, Schuster (1937), Hamilton-Paterson and Castleden (1942) Case 3, Our case 3

N C S * Marty and Froncin (1924), Norris (1932), Higgins (1934), Wright (1937), Our case 4

L C S * Scott (1924) Case 2, Abbott (1932), Benson, Hunter, and Manlove (1933) Case 2, Snyder and Hunter (1934) Case 1, Ostrum, Robinson, Nichols, and Widman (1938) Case 5, Chipps (1941)

MORBID ANATOMY

The figures below refer to the number of cases in which the feature mentioned has been recorded, since the descriptions are often insufficient, the figures are necessarily incomplete

Congenital Aneurysms (25)

Sinus involved   R C S 20, N C S 5, L C S 0
Origin from sinus   Sac with round or oval opening 0 5 to 1 5 cm sinus not dilated, 12   Whole

sinus dilated, no separate aneurysmal sac, 2 Both dilated sinus and aneurysmal sac 2

Position of opening in sinus   R C S right half, 3 central, 2, left half, 4   N C S   Adjacent to R C S, 3, central, 2

Size   None larger than 4 cm diameter

Shape   Globular, unless ruptured, then collapse, unless thickened, to form fistulous channel 1 5 to 2 5 cm long

Walls   Thin, often transparent, but occasionally thickened

Cardio-aortic fistulæ   R C S 17 led to fistulæ, 13 to conus of right ventricle, 2 to right atrium, 1 to left ventricle, 1 to pulmonary artery Fistulæ due to rupture of aneurysm, 12   probably present from birth, 5   N C S 4 ruptured into right atrium   No congenital aneurysm ruptured outside heart

Encroachment on intracardiac structures   R C S Pulmonary valve, 6, tricuspid valve, 5   ventricular septum, 2, right ventricle, 1, both ventricles, 1   N C S   Right atrium 5, tricuspid valve, 3, conducting bundle, 1

Aortic incompetence   R C S 4

Associated lesions   Congenital   23   Anomalies of aortic cusps, 15 (bicuspid, 6, much enlarged cusp, 4, rudimentary cusp, 1, thickened cusp, 4, calcified cusp, 2, fenestrated cusp, 2) Subaortic stenosis, 2   Abnormal extension of annulus fibrosus, 2   Ventricular septal defects, 10 (bulbar, 3, probably bulbar, 6, ruptured ventricular septal aneurysm, 1)   Coarctation of the aorta, 2   Pulmonary conus stenosis 1 Single coronary artery, 1   Patent foramen ovale, 1

Acquired   Subacute bacterial endocarditis, 6 Rheumatic heart disease, 1

Cardiac enlargement   Myocardial hypertrophy, 20, enlargement both ventricles, 14, mainly left ventricle, 4, mainly right ventricle, 4

Heart weight   Less than 300 g, 3   350 to 450 g, 2, 500 to 650 g, 5

Summary   Congenital sinus aneurysms have been confined to the right coronary sinus and the adjacent two-thirds of the non-coronary sinus They are always small but owing to their thin walls, commonly rupture to form cardio-aortic fistulæ (21 of 25) usually communicating between the right coronary sinus and the right ventricle, or between the non-coronary sinus and the right atrium They remain entirely intracardiac and do not affect extracardiac structures nor rupture outside the heart, but frequently cause disturbance of intracardiac structures, especially the pulmonary

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* R C S Right coronary sinus   N C S Non-coronary sinus   L.C S Left coronary sinus
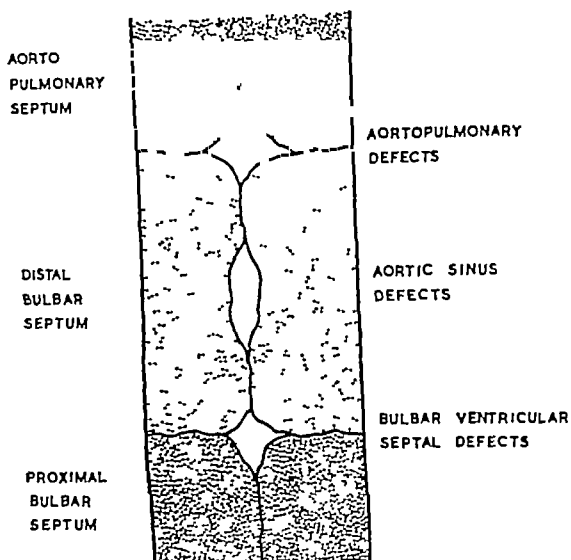
FIG 9 —*Formation of the bulbar septum* Fusion of the aortico-pulmonary and the proximal and distal bulbar septa occurs last at the areas represented as gaps The suggested defects which may arise at these sites are indicated on the right

FIG 10 —*Formation of the aortic cusps* Growth of the cusps indicated by interrupted lines Only two cusps can be related to the bulbar septum

valve, which is often interfered with by right coronary sinus aneurysms, and the tricuspid valve which may be encroached upon by aneurysms arising in either sinus Congenital sinus aneurysms are nearly always associated with other developmental faults, usually anomalies of the aortic cusps or bulbar ventricular septal defects Apart from bacterial endocarditis, acquired heart disease has occurred in only one case

Acquired Aneurysms (22)

Ætiology Associated with syphilis, 17, with bacterial endocarditis, 4, dissecting, 1, atheromatous, 1

Sinus involved R C S 11 N C S 5 L C S 7

Size Often very large, e g admitting two fists

Rupture R C S 7 (right ventricle, 1, pulmonary artery, 2, pericardium, 1, left pleural cavity, 1, externally, 2) N C S 3 (right atrium, 2, pericardium, 1) L C S 1 (pulmonary artery)

Encroachment of intracardiac structures R C S Pulmonary artery, 1, right coronary artery, 4, tricuspid valve, 1, septum and conducting bundle, 1 N C S 0 L C S Pulmonary artery, 2, left atrium, 3, left coronary artery, 2, left ventricle, 1, mitral valve, 2

Associated lesions Aortic incompetence, 8 (syphilitic, 6, bacterial endocarditis, 2) Bicuspid aortic valve, 2

2A

Summary Acquired sinus aneurysms may arise from any of the aortic sinuses Owing to their large size they tend to extend upwards, often becoming extracardiac and rupturing outside the heart Cardio-aortic fistulæ were present in only 6 cases They encroach upon intracardiac structures less often than congenital aneurysms Congenital cardiac defects were present in only two cases, but acquired heart disease was invariably present, usually syphilis or bacterial endocarditis

EMBRYOLOGY

Congenital sinus aneurysms are believed to arise from defective development of the distal bulbar septum This structure separates the systemic and pulmonary halves of the bulbus cordis, the primitive exit tube of the heart It arises by endothelial outgrowths from each side of the bulbus cordis, and is completed by fusion distally with the aorto-pulmonary septum and proximally with the proximal bulbar septum, which represents the bulbar part of the ventricular septum (Fig 9)

Congenital weaknesses are likely to develop at points of fusion, that is, distally, where the distal bulbar septum fuses with the aorto-pulmonary septum, between the two halves of the distal bulbar septum, and proximally where the distal meets the proximal bulbar septum (Fig 10) It is reasonable to suppose that congenital aorto-pulmonary fistulæ

develop at the distal site, aortic sinus aneurysms and cardio-aortic fistulæ at the intermediate site, and bulbar septal defects at the proximal site of fusion

Although all the aortic sinus aneurysms collected by Abbott (1919) arose from the right coronary sinus, aneurysms undoubtedly arising from the non-coronary sinus have been subsequently reported, but there is no reported instance of a congenital aneurysm arising from the left coronary sinus From Fig 10 it is clear that only two sinuses can be related to the distal bulbar septum, so it is not surprising that these aneurysms are confined to the right coronary and non-coronary sinuses

Micks (1940) collected three cases of aneurysmal dilatation of all three aortic sinuses and added a new case, Brown (1939) also mentions a similar case Micks tentatively suggested that such cases might be of developmental origin, but since neither syphilis nor cystic medical necrosis was excluded by adequate histological examination in any of these cases, we do not regard their developmental origin as proven

CLINICAL FEATURES OF CONGENITAL SINUS ANEURYSMS

Patients with congenital sinus aneurysms are usually male (19 of 24)   Signs and symptoms might arise from (a) a cardio-aortic fistula, (b) interference with intracardiac structures, (c) other congenital defects, or (d) bacterial endocarditis

Cardio-aortic fistulæ A defect in the wall of an aortic sinus gives rise either to a congenital cardio-aortic fistula or to aneurysmal dilatation of the sinus that leads to a cardio aortic fistula by rupture later in life, signs and symptoms due to the fistula may therefore either be present from birth or appear suddenly in later life

Congenital cardio-aortic fistulæ Five of the twenty-one fistulæ are believed to be congenital In one case death occurred from pulmonary atelectasis ten days after birth and in another enterocolitis led to death at four months old, the aneurysms were incidental necropsy findings In two other cases cardiac symptoms were minimal until two months and three years prior to death from heart failure at ages of 30 and 31, both patients had multiple congenital cardiac lesions including septal defects The remaining patient never had cardiac symptoms, and death at age of 53 followed two weeks illness of unknown nature associated with severe vomiting and abdominal pain   Thus, death was due to intercurrent disease in three cases, and in the other two cases cardiac symptoms did not appear until the end of the third decade

Cardio-aortic fistulæ due to sinus aneurysm rupture Eppinger (1916) has described the event of rupture   A man of 43, previously fit and active, was climbing a mountain and bent down to lift a heavy stone, when about to cast this aside he was seized by a sudden pain in the chest and immediately noticed a " whirring " sensation in the mid-sternal area " like a half-filled bottle being shaken " in the chest   These sensations gradually diminished in severity and he was soon able to lead the way down the mountain   Eight days later he noticed difficulty in breathing and palpitation and soon became unable to walk more than a few steps, he was confined to bed and treated with digitalis without improvement, he developed œdema and died nine months later

Of 25 congenital aneurysms, 15 are believed to have ruptured during life, in 6 cases death followed within five weeks and 6 died between two and thirteen months   Of the remaining 3 cases, one died four years after rupture due to further tearing of the aneurysm, a second died nine years later from bacterial endocarditis, and the third (our Case 2) survived seventeen years with intermittent failure, eventually dying with lobar pneumonia

It therefore appears that the heart tolerates a congenital cardio-aortic fistula much better than its sudden development in later life, which usually leads to progressive heart failure, death occurring within a few weeks in over one-third of cases and within about a year in four-fifths of cases, in exceptional cases symptomatic recovery takes place, death being due to a second rupture or to intercurrent disease

The physical signs of a cardio-aortic fistula are an important feature of congenital sinus aneurysms for in only 4 of 25 cases was the aneurysm wall intact at death, in 13 cases the fistula led to the right ventricle, in 6 cases to the right atrium, in 1 case to the left ventricle, and there was an aorto pulmonary fistula in the remaining case

Both patency of the ductus arteriosus and aorto pulmonary communications (Shepheard, Park, and Kitchell, 1944) give rise to a systolic diastolic murmur at the base of the heart   and a collapsing pulse   But a communication between the greater and lesser circulations lying below the valve cusps as in ventricular septal defect causes only a systolic murmur   In cardio-aortic fistulæ one end of the fistula lies above the cusps, and one below, but there is no doubt that the associated murmur usually extends into diastole   This was so when there was no other congenital lesion (our Case 2) or only congenital lesions associated with systolic murmurs (10 cases)   The character of this systolic diastolic murmur is striking for it is often described as superficial, simulating pericardial friction, and

nearly always coarse, harsh or rasping in character, accompanied by a thrill, usually systolic, but in Abbott's (1919) case there was a diastolic thrill so intense that it could be felt through the bedclothes The systolic and diastolic components may merge into each other to form a continuous murmur so that the cardio-aortic fistula murmur is more likely to be confused with the murmurs of patency of the ductus or of a congenital aorto-pulmonary communication than with the to-and-fro murmurs of acquired aortic valve disease The cardio-aortic fistula murmur tends to be lower in position than other continuous systolic-diastolic murmurs, and it was definitely louder in the third or fourth spaces than in either the second space in 6 of 9 cases in which this is recorded The physical signs are essentially similar whether the fistula leads to the right ventricle or the right atrium In the case reported by Herson and Symons (1946) the physical signs are of exceptional interest for, at the age of 12, before rupture, there was only a loud musical systolic murmur, maximal at the inner ends of the fourth and fifth interspaces, presumably due to the associated ventricular septal defect, whereas after rupture at the age of 31 the typical systolic-diastolic murmur became audible

(b) *Interference with intracardiac structures* The *aortic valve* was often affected and was incompetent in 7 cases, probably due to distortion by the aneurysm in 4 cases There do not appear to have been striking symptoms until the aneurysm ruptured or bacterial endocarditis developed The *tricuspid valve* was involved in 8 cases In only 2 was a clinical diagnosis of tricuspid disease made, in these cases a systolic murmur was heard at the lower end of the sternum and hepatic pulsation was present In 2 others, the necropsy findings suggested significant interference with the tricuspid valve, but in all 4 the patients had apparently been well and active until their aneurysms ruptured thirteen months, one month, four and a half weeks, and ten days before death The *pulmonary valve* cusps were pushed aside in 5 cases, in none of these was pulmonary valve disease suspected during life, although pulmonary incompetence was diagnosed in another case in which the valve was not affected

Pressure on the conducting bundle was believed to have led to the complete heart block in one case and pressure on the A-V node was regarded as the cause of A-V nodal rhythm in the other case Encroachment upon the cardiac chambers has often occurred, but there is no evidence that it has impaired cardiac efficiency

(c) *Associated congenital cardiac defects* If a cardio-aortic fistula is present, its signs and symptoms overshadow those of other less striking con-

genital lesions, which can be studied only in cases with unruptured aneurysms and by reviewing the history prior to rupture in other cases In two cases with unruptured aneurysms no clinical details are available, and in the other two there were no symptoms until bacterial endocarditis developed in the one case and Stokes-Adams attacks in the other Of 15 patients whose aneurysms ruptured there were no cardiac symptoms prior to rupture in 14, and in the remaining one the incapacity was due to bacterial endocarditis Ventricular septal defects were present in 6 cases, aortic incompetence in 3 cases, and slight coarctation of the aorta in 2 cases The congenital defects associated with aortic sinus aneurysms appear to be of an almost asymptomatic type

(d) *Subacute bacterial endocarditis* Of 6 unruptured aneurysms, 4 became infected, 2 of these subsequently ruptured Of 13 aneurysms that ruptured during life only one subsequently became infected, and that nine years later The short duration of life after rupture may account for the rarity of subsequent infection None of the five congenital communications became infected Age does not appear to be a factor in determining the preponderance of infection in unruptured aneurysms, for the average age at death was similar in all groups and bacterial endocarditis developed at ages from one and a half to 56 years

CAUSES OF DEATH

Heart failure was the cause of death in 15 of 25 cases, and in 12 could be attributed to rupture, in 2 to congenital cardio-aortic fistulæ, and in 1 to rheumatic heart disease associated with an unruptured aneurysm *Bacterial endocarditis* led to death in 6 cases, and *intercurrent disease* was the immediate cause of death in 4 cases Thus, nearly two-thirds of these patients died from heart failure, usually due to the cardio-aortic fistula, and one quarter from subacute bacterial endocarditis

In this summary of the clinical features of congenital sinus aneurysms the signs and symptoms associated with a cardio-aortic fistula have been emphasized, for this complication is present in the majority of cases, dominates the clinical picture by its often dramatic onset and striking physical signs, and usually leads to heart failure which is the commonest cause of death By comparison, the effects of local extension of the aneurysm and the signs of other congenital defects are unimportant

RADIOGRAPHY

Congenital sinus aneurysms are usually small and almost always project into a cardiac cavity rather than externally It is therefore not surprising

to find that, in six published cases in which radio-logical findings are given, and in our two cases, no evidence of localized aneurysmal swelling was observed   Roesler (1943) and Ostrum *et al* (1938) have described small projections from the vascular pedicle, often evident only in the oblique views, in cases of sinus aneurysm, but we conclude that these observations relate to the acquired variety   In eight cases with radiological findings, the heart was enlarged in all   In seven of them a cardio aortic fistula was present and probably responsible for the enlargement, in the remaining case a ventricular septal defect and aortic incompetence were present The available evidence indicates that the enlargement involves both ventricles   The aortic shadow was not abnormal in four cases where this point is recorded

ELECTROCARDIOGRAPHY

Only two electrocardiograms have been published, and the findings are described in three other cases Including our two cases, we have information about the standard limb leads in only seven cases   In two cases right axis deviation was associated with signs suggestive of aortic incompetence, though actually due to the cardio-aortic fistula, some diagnostic significance was assigned to this associa-tion by Hirschboeck (1942) and Herson and Symons (1946) but it has not occurred in the other cases, left axis deviation being present in three cases Complete heart block and auricular fibrillation have each occurred in one case   The electrocardiographic findings are so inconstant that they give little assist-ance in diagnosis

DIAGNOSIS OF CONGENITAL SINUS ANEURYSMS

An unruptured congenital aortic sinus aneurysm is almost asymptomatic and without physical or radiographic signs, though the presence of congenital heart disease may be recognized by the signs of an associated lesion such as a bulbar septal defect Unruptured sinus aneurysms are, however, very prone to become infected, as we have shown, and when bacterial endocarditis develops in a heart apparently previously healthy, this is one of the silent underlying lesions that may be suspected

The situation is quite different when a cardio-aortic fistula is present, either congenital or due to the rupture of a sinus aneurysm, for this is associated with striking physical signs and, if due to rupture in later life, with a dramatic clinical history   Eppinger (1916) was able to make a correct clinical diagnosis in his case by comparing the event of rupture during effort and the physical signs that followed with the similar case described by Kraus (1902)   Rupture of

a congenital sinus aneurysm is perhaps most likely to be confused with rupture of an aortic cusp though this is usually associated with either syphilis or bacterial endocarditis   If these two diseases can be excluded rupture of a sinus aneurysm may justifiably be suspected, unless it is to be admitted that a healthy aortic cusp can rupture owing to exceptional trauma   In this differential diagnosis the physical signs will be helpful for the characteristic harsh, superficial, systolic-diastolic murmur often accompanied by a thrill, maximal in the third left interspace near the sternum should differentiate a cardio-aortic fistula from aortic incompetence but the accompanying Corrigan pulse gives little help for it is present in both conditions

It is more doubtful whether a precise diagnosis can be made when the cardio-aortic fistula is present from birth for the advantage of the characteristic history of rupture is lost   The nature of the mur-murs and their presence from early life will suggest a *congenital heart lesion but it will almost certainly be impossible to distinguish between an aorto-pulmonary fistula and a cardio-aortic fistula* and the differential diagnosis from patency of the ductus arteriosus may be difficult   The more superficial and harsher murmurs situated unusually low for that of a patent ductus, and the more striking Corrigan pulse, may lead to the suspicion of a cardio-aortic fistula, but these qualities are merely a matter of degree and it must be admitted that no reliable differential sign is available   Electrocardio graphy and radiography will give little help unless an enlarged pulmonary artery suggests patency of the ductus, for it has not occurred in aortic sinus aneurysms   Since surgical ligation of the ductus has become commonplace, it is fortunate that congenital cardio-aortic fistulæ are rare

SUMMARY

The nomenclature of the aortic sinuses is discussed and the topography of the aortic root illustrated

Four cases with aortic sinus aneurysms two congenital and two due to *aortic disease* are described

Including these cases, a verified series of 25 con-genital and 22 acquired sinus aneurysms has been collected

The pathological features of the condition are illustrated by an analysis of this series of cases

The embryology of congenital sinus aneurysms is briefly discussed

The clinical features of congenital sinus aneurysms are described and diagnosis is discussed   *Attention is directed to the striking clinical features associated* with a cardio-aortic fistula

When a congenital sinus aneurysm ruptures in later life we may, from the combination of history and physical signs, expect to recognize the presence of cardio-aortic fistula, if a congenital cardio-aortic fistula is present the existence of a congenital heart lesion will be manifest and, from the physical signs we may suspect the presence of a congenital cardio-aortic fistula or an aorto-pulmonary communication Finally, although we cannot hope to diagnose an unruptured aortic sinus aneurysm, it is, like a bicuspid aortic valve, one of the silent congenital lesions to be suspected when bacterial endocarditis develops in a heart apparently previously healthy

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THE Q–T INTERVAL IN ACUTE RHEUMATIC CARDITIS

BY

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In the initial stages of rheumatic fever, carditis can usually be diagnosed with ease, since the significant murmurs are almost always to be heard In the presence of polyarthritis, pyrexia, and raised sedimentation rate, it can be safely assumed that this carditis is active   It may, however, be extremely difficult to determine how long such activity persists the temperature and pulse rate may be normal, the electrocardiogram may show no gross changes, and such laboratory tests as are performed may show no abnormality, and yet, in some of these cases, it seems probable that carditis is still active This study is an attempt to use electrocardiographic data to supply criteria of such sub-clinical activity

Donders (1868) originally studied the duration of systole on the radial plethysmograph   Two years later Garrod (1870), using the same technique, evolved a formula for correcting the first, or systolic portion of the plethysmograph, for heart rate, and suggested that alterations in the duration of systole might be useful in the diagnosis of heart disease

Berliner in 1931 first noted that prolongation of the Q–T interval of the electrocardiogram occurred in rheumatic valvular disease   Drawe *et al* (1937) measured the Q–T interval in 100 rheumatic and 100 normal children   They showed that 25 per cent of the former and 4 per cent of the latter were above the upper limit of normal as judged by Ashman and Hull's (1937) criteria   They did not state, however, whether acute carditis was present when this measurement was taken   Taran and Szilagyi (1947) found that the duration of electrical systole, both absolute and relative to diastole, was significantly lengthened in all cases of acute rheumatic carditis   They further stated that this prolongation was not a function of the cardiac rate, but rather of the severity of the disease, that this prolongation preceded all other laboratory criteria of rheumatic activity, and that it did not return to normal until long after all other diagnostic signs had reverted to normal

In view of the importance of this statement an investigation was undertaken to see whether prolongation of the Q–T interval was a reliable index of active carditis and whether it could prove of prognostic significance

MATERIAL

In all, 134 cases were studied   The patients were under treatment in the special unit for juvenile rheumatism at the Canadian Red Cross Memorial Hospital, Taplow, no special selection of cases was made   Some were local patients, admitted in the initial stages of the rheumatic attack, but the majority were transferred from other institutions, provincial and metropolitan, throughout Great Britain, where they had already been under treatment for varying periods of time   The majority of the patients were children (see Table I)

TABLE I

AGE DISTRIBUTION

0– 5 years	6 cases
6–10 years	56 cases
11–15 years	50 cases
16–20 years	13 cases
Over 20 years	9 cases

On admission to hospital the cases were divided clinically into one of three main groups, those presenting evidence of active carditis those presenting evidence of inactive carditis, and those cases in which no clinical carditis was detectable   Carditis was diagnosed clinically by the presence of one or more of the following   a diastolic murmur cardiac enlargement, the presence of a pericardial friction rub, tachycardia out of proportion to elevation of temperature, and grosser electrocardiographic changes such as prolongation of P–R interval Activity was recognized by pyrexia, tachycardia, and raised sedimentation rate

The group of cases of active carditis was further subdivided into those patients who showed a steady

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uninterrupted recovery and those who showed evidence of prolonged rheumatic activity

TABLE II

CLASSIFICATION ACCORDING TO DEGREE OF CARDITIS OR ABSENCE OF CARDITIS

1 *Carditis*
   (i) Active carditis
      (*a*) Uninterrupted recovery   55 cases
      (*b*) Prolonged activity   45 cases
                                  100 cases

   (ii) Inactive carditis   12 cases

2. *No carditis*   22 cases
                           134 cases

METHODS

All electrocardiograms were taken on an American Cambridge continuous film electrocardiograph The time marker was accurately checked against an oscillator of known frequency All recordings were taken with the patient semi-recumbent at an angle of thirty degrees to the horizontal, Lombard and Cope (1919) having shown that systole varied with posture, being longer in the standing position

The absolute Q-T interval varies slightly from complex to complex, as does the cycle length, but Katz (1921) showed that, while cycle length and the length of systole may vary phasically, these variations are not synchronous nor of like degree To obviate distortion of cycle length by sinus arrhythmia, which in some cases was marked, the heart rate was calculated by counting the complexes over the entire length of tracing taken, covering at least two-thirds of a minute and usually one minute The average cycle length was then calculated from the heart rate

The Q-T interval was measured from the beginning of the Q wave until the end of the T wave in the standard lead in which the T wave was highest This was usually lead two At least six complexes were measured with calipers under a magnifying lens and the average length of the Q-T interval was taken

The absolute duration of Q-T depends upon the heart rate, and thus measurements must be corrected for heart rate before they can be compared Numerous formulae exist for this correction (Lombard and Cope, 1919, Fridericia, 1920, Ashman and Hull, 1937, Schlamowitz, 1946) All these formulae have been criticized, but the square root formula devised by Bazett (1920) is generally agreed to be one of the most reliable, and, because of its simplicity, has been used in this study Taran and Szilagyi (1947) used Bazett s formula but expressed it as

$$K = \frac{Q-T}{\sqrt{C}}$$ [where C=cycle length] They called K

the corrected Q-T or Q-Tc for short This method and nomenclature have been adopted here

Various values for the upper limit of Q-Tc have been laid down by different workers, Bazett (1920), Hegglin and Holzman (1937), Ashman and Hull (1937), and Taran and Szilagyi (1947) For this study electrocardiograms were taken on a short series of normal subjects, the upper limit of normal for Q-Tc was found to conform to Ashman and Hull's criteria which, accordingly, were adopted Therefore the upper limit of the normal for Q-Tc has been taken as 0 422 second for men and children and 0 432 second for women

RESULTS

(1) *Q-Tc and heart rate* It is imperative that any formula which is employed to correct Q-T for cycle length must not be distorted by extremes of heart rate Bazett's formula was tested as shown in Fig 1, in which 426 measurements of Q-Tc from
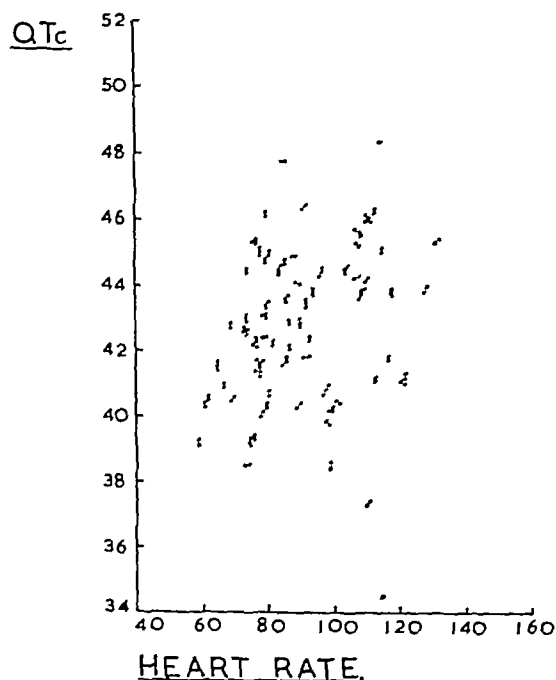
FIG 1 —Q-Tc correlated with heart rate

80 patients, both with and without carditis, are plotted against the heart rate

The longest values for Q-Tc occurred with neither the slowest nor the most rapid heart rates, but did in fact appear at heart rates between 80 and 120 In the presence of active carditis it is natural that this degree of tachycardia should obtain

TABLE III

RELATION OF QTc TO PRESENCE OF CARDITIS AND
TO ITS DEGREE OF ACTIVITY

| | Number of cases with carditis | | Number of cases without carditis |
	Active	Inactive	
Q–Tc prolonged	90	5	11
Q–Tc normal	10	7	11
Total	100	12	22

(2) *Q–Tc correlated with carditis* Table III shows that the Q–Tc was prolonged in ninety of a hundred cases of active carditis In the remaining ten cases the Q–Tc was within normal limits Two of these patients had suffered previous pericarditis which was shown by Tung (1941) to shorten Q–Tc In the remaining eight cases no factor was present that is known to shorten the Q–Tc In this series the upper limit of normal was taken as 0 422 second for children as opposed to 0 405 second used by Taran and Szilagyi (1947) This may explain why only 90 per cent of these cases of active carditis showed a prolonged Q–Tc against 100 per cent in Taran and Szilagyi's series Out of twelve cases with rheumatic heart disease, which were considered inactive on admission, five showed

a prolonged Q–Tc There was no other evidence of active carditis, but data given later in this paper tend to prove that this did exist Of twenty-two cases considered to show no evidence of a heart lesion clinically, eleven cases showed a prolonged Q–Tc Four of these cases were shown to have suffered carditis by the subsequent appearance of significant murmurs It therefore seems probable that some of the remaining seven patients in this group suffered minimal cardiac damage, unrevealed by any of the criteria upon which a clinical diagnosis of carditis was made

(3) *Q–Tc variation during the course of rheumatic fever* The behaviour of Q–Tc was studied, both in patients making a rapid recovery from the rheumatic attack (Table II, Group (a)) and those showing prolonged rheumatic activity (Group (b)) The behaviour of Q–Tc in six cases belonging to Group (a) is shown in Fig 2 and demonstrates the return of Q–Tc to normal with recovery

Fig 3 shows the behaviour of a typical Group (a)

FIG 2 —Behaviour of Q–Tc in six cases in Group 1 (a)
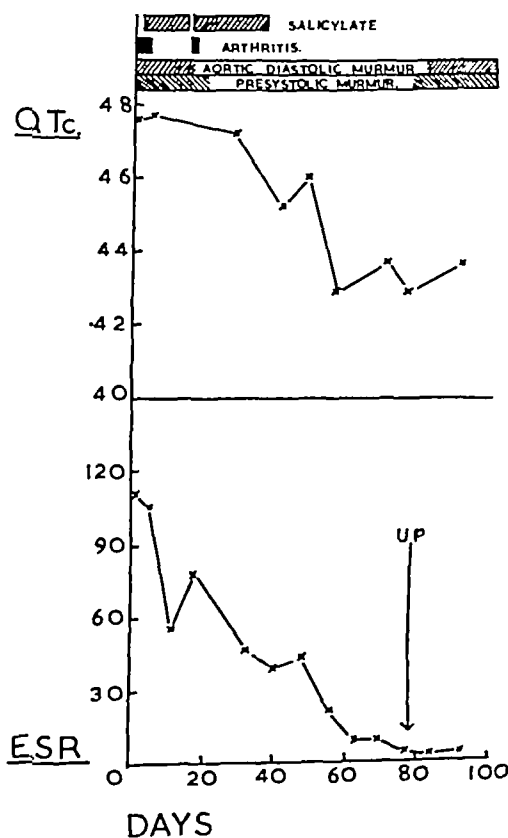
FIG 3 —Behaviour of Q–Tc in a typical case in Group 1 (a)

case   This patient was admitted in the initial stages of her third attack of rheumatic fever   Mitral stenosis, due to previous rheumatic carditis, was present as witnessed by a presystolic murmur   On admission the sedimentation rate was raised and the Q-Tc was grossly prolonged, which was taken as evidence of acute carditis in this attack   With recovery her Q-Tc reverted to normal

Fig 4 and 5 demonstrate the behaviour of Q-Tc in two patients of Group (*b*) showing evidence of prolonged rheumatic activity, or what may be called chronic rheumatic carditis   Fig 4 shows that although the sedimentation rate came down to normal occasionally, the Q-Tc was prolonged for the whole of the 240 days covered by the graph Prolongation of Q-Tc may occur in chronic rheumatic heart disease without active carditis   This will be discussed later

Fig 5 illustrates another case in Group (*b*), in this instance complicated by congestive failure Two points should be noted   the steady fall in sedimentation rate with the onset of congestive failure, and the rapid shortening of Q-Tc on two occasions when digitalis was exhibited   This effect was noted by Cheer and Dieuaide (1931) This latter point is also illustrated by Fig 6 which

shows the shortening of Q-Tc in two normal patients when digitalis was exhibited   In neither of these patients was the direction of the T wave seen to change in the electrocardiograms subsequent to the administration of digitalis

Fig 7 illustrates the effect on Q-Tc of an exacerbation of rheumatic carditis   When admitted, this patient was judged to be quiescent, following a second attack of rheumatic fever   The antistreptolysin titre was 150 units, the sedimentation rate was normal, and the Q-Tc was not prolonged Established heart disease was present and rheumatic nodules were noted   He then developed scarlet fever, the Q-Tc immediately rose and at the same time the P-R interval lengthened from 0 16 to 0 27 sec   The antistreptolysin titre rose to 400 and later to 833 units   The sedimentation rate also rose and he suffered a severe exacerbation of carditis The P-R interval first came back to normal, this was followed by a return to normal of the sedimentation rate   The Q-Tc, however, remained prolonged In the present series the P-R interval was always found to be normal when the Q-Tc was within normal limits

(4) *Correlation of Q-Tc and sedimentation rate* The sedimentation rate still remains one of the most
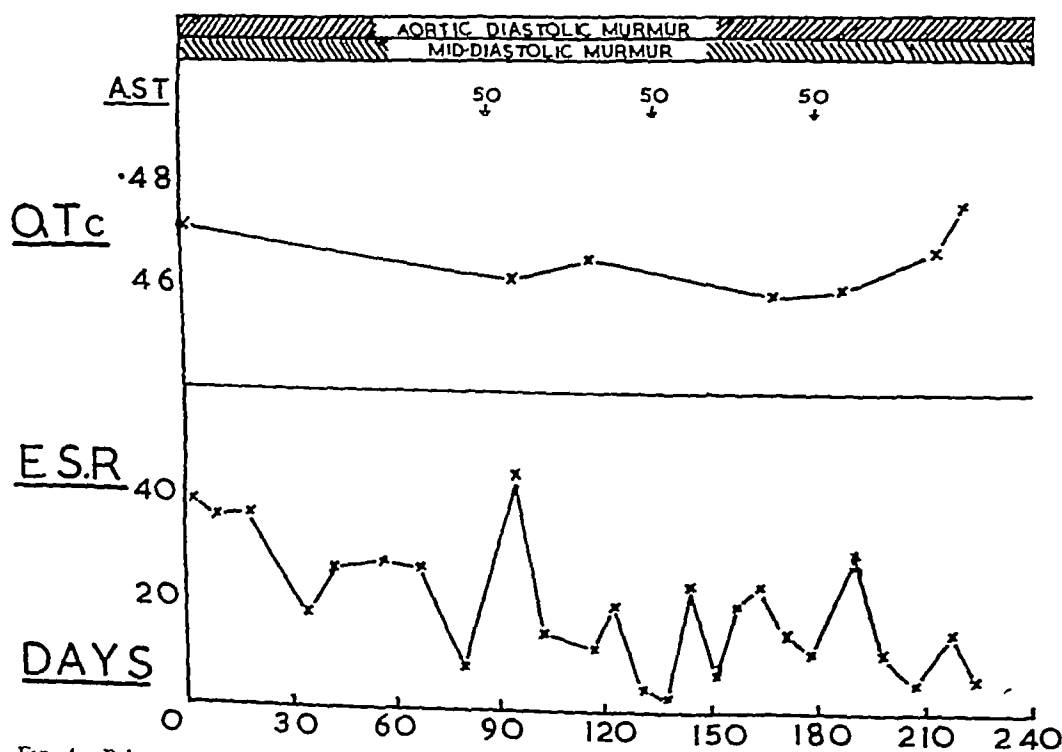
FIG 4 —Behaviour of Q-Tc in chronic rheumatic carditis   Group 1 (*b*)   A.S T =Antistreptolysin " O " titre
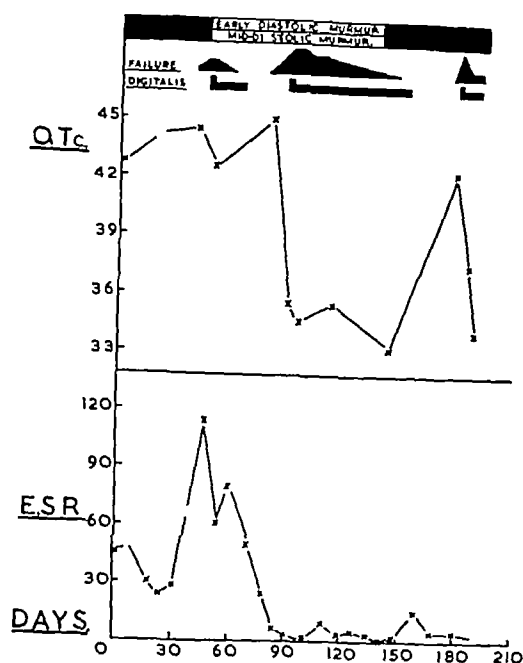
FIG 5 —Behaviour of Q–Tc in another case with chronic rheumatic carditis   Note influence of digitalis on the length of Q–Tc and the fall in ESR with the onset of congestive failure
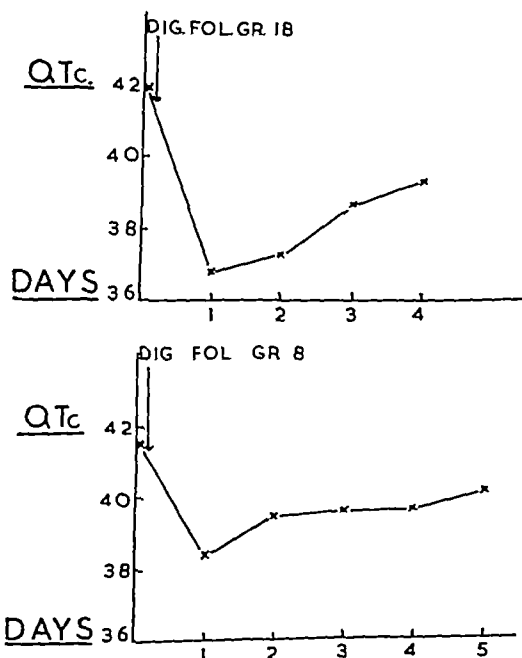
FIG 6 —Effect of digitalis on Q–Tc in normal subjects
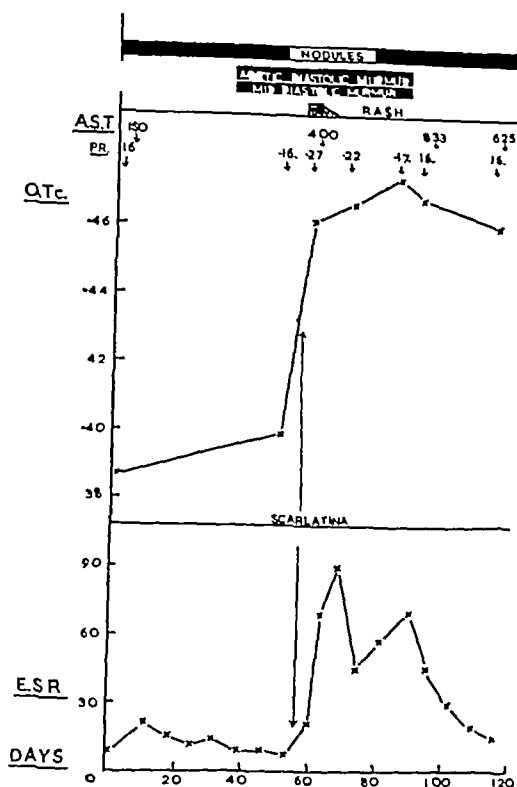
FIG 7 —Recurrence of rheumatic carditis and Q–Tc PR = P–R interval in seconds

important signs of rheumatic activity, accordingly, the duration of Q–Tc was compared with the sedimentation rate in patients with, and without, carditis   The results are illustrated in Fig 8

In Fig 8, 293 readings of Q–Tc from sixty patients with active carditis are plotted against the sedimentation rate on a semi-logarithmic scale and it will be seen that in general, the length of Q–Tc varies directly as the sedimentation rate   It will be noted, however, that some patients with active carditis show a short Q–Tc in spite of a high sedimentation rate, some of these patients were suffering from pericarditis, and others were receiving digitalis, the effect of this drug on systole being well known   It will also be observed that the Q–Tc was frequently prolonged when the sedimentation rate was within normal limits   Such observations were made towards the end of the patients' stay in hospital, and illustrate the persistence of a long Q–Tc at a time when other evidence of activity, such a the sedimentation rate, had subsided

Fig 9 shows 36 readings of 11 patients with
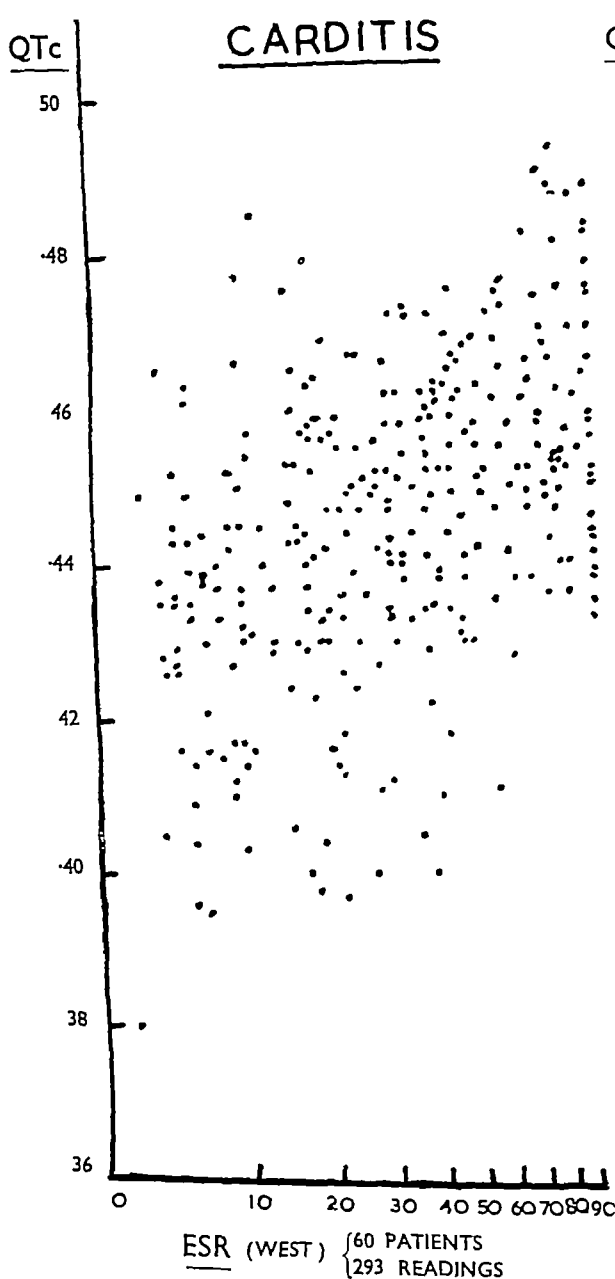
FIG 8 —Correlation of Q-Tc with ESR in patients with active carditis   Compare Fig 9

FIG 9—Correlation of Q-Tc with ESR in patients with acute rheumatic fever without carditis

acute rheumatic fever, but no clinical evidence of carditis, the Q-Tc is below the upper limit of normal in every case, and bears no relationship to sedimentation rate

(5) *Q-Tc and relapses*   These findings confirm Taran s claim that prolongation of Q-Tc is a reliable index of active carditis   It follows therefore that increase in physical activity in the presence of a prolonged Q-Tc might theoretically be expected to precipitate a relapse   The relapses that occurred were analysed accordingly   Fig 10 illustrates this point

This child was admitted in the middle of a severe attack of rheumatic carditis   The Q-Tc was grossly prolonged, the sedimentation rate was raised, erythema marginatum was noted, and a crop of nodules appeared   After 90 days in hospital the Q-Tc and the sedimentation rate were within normal limits   At this point she suffered another β-hæmolytic streptococcal infection, which was followed by a severe exacerbation of carditis, the Q-Tc rose and a slower rise in sedimentation rate occurred   Rash and nodules re-appeared   Two hundred and sixty days after admission the sedimentation rate, temperature, and pulse rate had returned to normal   She was then considered clinically inactive and was allowed up, in spite of a prolonged Q-Tc   An immediate relapse followed, accompanied by a further rise in Q-Tc and sedimentation
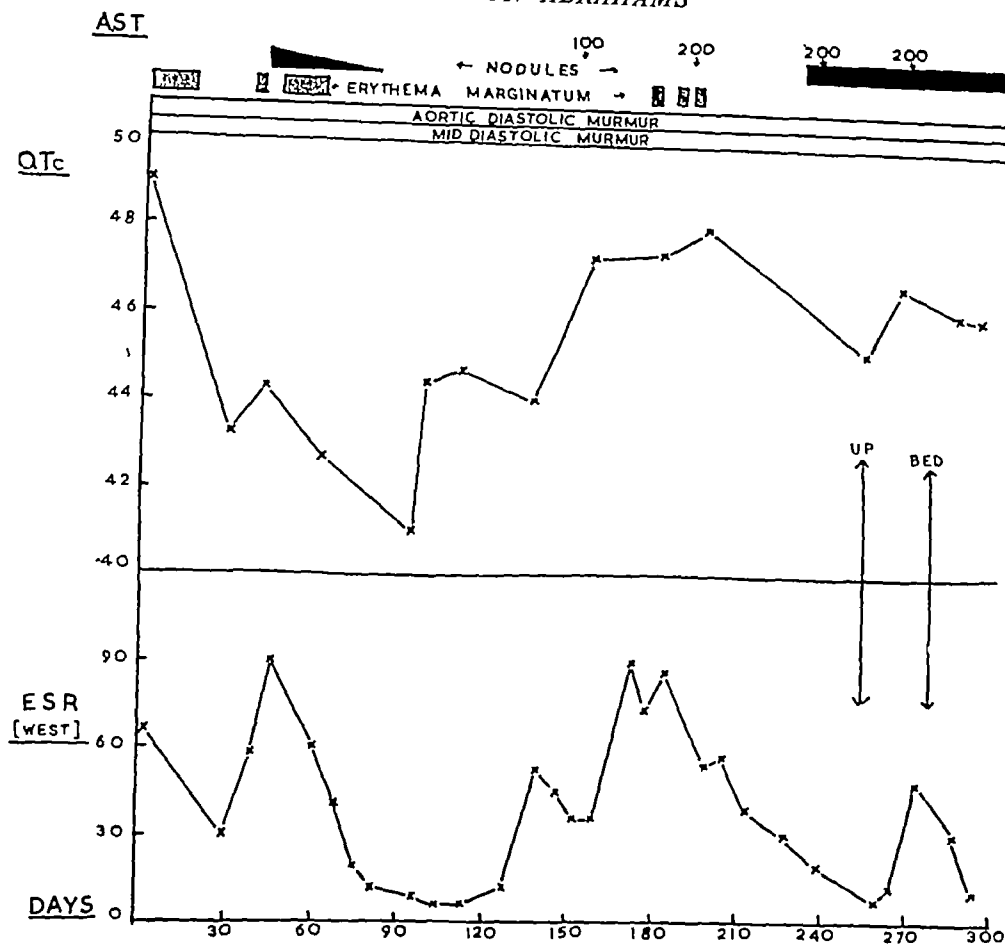
FIG 10 —The effect of an increase in physical activity in the presence of a prolonged Q-TC

rate, necessitating return to bed The anti-streptolysin titre of 200 throughout this episode was very strong evidence against an occult streptococcal re-infection and subsequent rheumatic recurrence

The criteria for judging an exacerbation of rheumatic carditis to be a relapse, rather than a recurrence, must be specified and adhered to rigidly In much of the present series essential data were not obtained and definite conclusions could not be drawn However, of twenty patients who apparently relapsed, fifteen were noted to have a long Q–Tc at the time that physical activity was increased There was no other evidence of active carditis in any of these patients This and other material is now under careful analysis to find out whether prolongation of Q–Tc at the time that physical activity is increased is a significant factor in causing relapses

DISCUSSION

These results prove that prolongation of Q–Tc occurs in active rheumatic carditis, but throw no light on the mechanism of its production It is extremely doubtful if alterations in the diastolic filling pressure, or in the diastolic volume of the cardiac chambers, can be responsible, as in the majority of cases the venous pressure is not raised clinically Prolongation of systole due to biochemical causes may be similarly discounted In the patients who make an uninterrupted recovery from an attack of rheumatic carditis, it would appear that this prolongation depends upon actual involvement of the myocardium by the rheumatic process

In chronic cases where the heart suffers prolonged myocardial and valvular damage other factors are involved In this group, actual muscular hypertrophy of the heart, consequent on valvular

deformity, may be responsible in part for prolonging Q-Tc. Even minor degrees of ventricular hypertrophy may now be detected by modern electrocardiographic methods. Prolongation of Q-Tc due to this cause has been noted by Berliner (1931) and Drawe *et al* (1937). Comparable lengthening occurs in hypertensive heart disease, in cardiac failure from any cause, and in some cases of congenital heart disease, in particular, pulmonary stenosis. In all these conditions hypertrophy of the heart may occur and it seems possible that this increase in the bulk of heart muscle may lead to prolongation of Q-Tc. In cases in which the rheumatic process runs a severe and protracted course, giving rise to detectable ventricular hypertrophy, it would be unwise to ascribe prolongation of Q-Tc entirely to active carditis, especially when other signs of rheumatic activity are absent.

First degree heart block was noted in a number of patients. The incidence of this complication was not greater than has been previously described. It was noted, however, that prolongation of the P-R interval never occurred when Q-Tc was within normal limits, although the reverse obtained very frequently.

Until more complete data are available it does not seem justifiable to enforce long periods of bed rest when a long Q-Tc is the only abnormal finding.

Further work on this aspect of the problem may be of great help in assessing the degree of physical activity that may safely be permitted in the individual case.

SUMMARY AND CONCLUSIONS

Prolongation of Q-Tc is a valuable index of active carditis in rheumatic fever, and active carditis may be detected by the presence of a prolonged Q-Tc long after all other clinical and laboratory criteria of activity have gone.

Prolongation of Q-Tc may be the only evidence of cardiac involvement in acute rheumatic fever.

In chronic rheumatic carditis, prolongation of Q-Tc may be due to causes other than active carditis.

Measurement of Q-Tc may be of help in assessing the degree of physical activity that may be allowed in the individual case.

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A CLINICAL TRIAL OF RAUWOLFIA SERPENTINA IN ESSENTIAL HYPERTENSION

BY

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In a casual perusal of papers on hypertension, one comes across well over a hundred so-called hypotensive remedies alleged to possess the property of lowering the blood pressure   In 1930, Ayman could collect over two hundred reports on the successful treatment of hyperpiesia by various hypotensive remedies

In view of the persistently high mortality from hypertension in spite of the large number of measures recommended in the treatment of this disease one is forced to admit the futility or helplessness of the situation   In Ayman's opinion, the "proper treatment is still unknown"   Evans and Loughnan, after a critical analysis and trial of thirty-three different preparations in seventy cases of high blood pressure (essential hypertension), were forced to admit the uselessness of them all   In their opinion, simple sedative measures are often more effective than the much more expensive and fashionable products extensively displayed on the market

There is unfortunately, a great tendency on the part of both the medical profession and the laiety, to hail or applaud any new drug or measure introduced into the market, often on the basis of a few stray experiences or clinical impressions   In consequence of this attitude, many of the present day clinicians have learnt not to accept any claim for a new remedy unless and until its therapeutic value has been firmly established by resort to carefully controlled clinical observations

My selection of *R Serpentina* for the present study has not been entirely fortuitous   I have been prompted into the present enquiry by several factors   In the short span of ten years that the dried root of *R Serpentina* has been on the market in India, in tablet form, there has been a growing demand in this country for these tablets   Preparations of the serpentina root have gained such unprecedented popularity for hypertension cases in this country, that there is hardly a patient with high blood pressure who has not been subjected to its effects in one form or another   One manufacturing firm alone claims to have sold over 50 million tablets of the dried root   One of the aims of the present investigations has therefore been to determine if this enthusiastic reception of the drug is warranted   As early as 1940, I had made the following allusion to the subject of *R Serpentina* treatment in cases of hypertension   "After a trial of this preparation one finds it useful in a percentage of cases of hypertension only, the indications and suitability of the case for the drug have not as yet been worked out"   Since that time, I have had the opportunity of observing the effects of this drug in a very large number of cases   After an extensive trial of various hypotensive remedies in several thousand cases of hypertension, both in private and hospital practice during the last ten years, I have found *R Serpentina* to be the most consistently successful member of the whole group of hypotensive remedies   In reply to a recent questionnaire issued by me to fifty physicians from all over India, forty-six voted for *R Serpentina* as being the best "hypotensive   in their experience

In view of this overwhelming body of support in favour of regarding *R Serpentina* as the remedy of choice, I have considered it opportune to subject this preparation to a more critical analysis and to try and form an unbiased opinion of its value as a hypotensive agent   In the present investigation I have tried to steer clear of those fallacies involved in the interpretation of therapeutic results to which particular attention has been drawn by Ayman Kapernick, and others   There is an unfortunate tendency to claim success in the treatment of essential hypertension merely on the basis of symptomatic improvement   In the opinion of Ayman, the successful treatment of hyperpiesia, implies, of neces-

sity, a substantial reduction in the level of the blood pressure In Kapernick's opinion, "although symptomatic response is relatively easily obtained, reduction of blood pressure is difficult" This has been the experience also of Evans and Loughnan, who found that although good symptomatic relief can be obtained in cases of hypertension with a large number of remedies, the much more desirable hypotensive effect is rarely noted The factor of natural lability of the blood pressure, so common in hypertensives, is often lost sight of, in the interpretation of results, as a result, perfectly normal or natural fluctuations are mistaken or misconstrued for evidences of the therapeutic value of the drug under trial

According to Evans and Loughnan, any remedy before it can be accepted as having established a claim as a hypotensive agent must satisfy certain standards of efficiency, viz (1) it should be capable both of reducing a blood pressure that is high and of maintaining it at the lowered value, (2) it should be able to exhibit its hypotensive action consistently and in a high proportion of patients, and (3) it should be free of all toxic ill-effects

An Introduction to Rauwolfia Serpentina

The use of vegetable extracts in the treatment of high blood pressure is not new Both, watermelon seeds and the mistletoe plant have been tried in the past, without gaining general endorsement In 1939, Graham had reported benefit in cases of hypertension from the use of the tincture of hawthorne (*Crataegus oxycantha*)

R Serpentina (variously known in India as sarpagandha, chandrika, chotachand, chandra, dhanmarna, dhan-barua, patala-gandhi, and covanamilpori) or the Serpentina plant is a large climbing or twining herb or shrub, belonging to the natural order *Apocynaceæ*, and found in the Himalayas, in Assam, Pegu, Tennasserim, Java, the Deccan peninsula, and the Malaya peninsula

The root of this plant has been popular, both in India and in the Malay peninsula, from ancient times, as an antidote to the stings and bites of insects and poisonous reptiles It has been used also as a febrifuge, as a stimulant to uterine contractions, for insomnia, and most of all for insanity More recently, its clinical application has been extended, with success, to cases of high blood pressure

Early researches on *R Serpentina* showed that it contained an alkaloid which was provisionally called pseudobrucine On account of its popularity with practitioners of indigenous medicine, the chemical composition of the serpentina plant has been subjected to considerable scrutiny Sen and Bose (1931) discovered two alkaloids in its root, the total alkaloid content being about 1 per cent of the dried root, there being also a lot of resin and starch Siddiqui and Siddiqui (1931) found, besides phytosterol, oleic acid, and unsaturated alcohols, five alkaloids, which were classified by them into two groups, viz (1) The ajmaline group of three white crystalline, weak bases, ajmaline, ajmalinine, ajmalicine, and (2) the serpentine group of two yellow crystalline stronger bases, serpentine and serpentinine

On the basis of experiments on frogs, Siddiqui and Siddiqui showed that the ajmaline group acts as a general depressant to the heart, respiration, and central nervous system, whilst the serpentine group causes paralysis of respiration, depression of nerves, and stimulation of the heart Sen and Bose studied the pharmacological effects of the *R Serpentina* alkaloids on cats and other higher animals They reported a small drop of blood pressure, a stimulation of the respiration, a depression of the heart muscle and a relaxation of plain muscle-tissue (e g of the uterus and intestines) Roy (1931) found that large doses induce sleep, cause dulling of sensations and diminution of reflexes Fatal doses caused death from respiratory failure the heart continuing to beat for some time after Chopra has been engaged in pharmacological researches on the *R Serpentina* since 1932, but the results of his work are not as yet known It is claimed by certain manufacturers that the root from a well-reared and scientifically cultivated serpentina plant yields about three times more of the active alkaloids than the root from the wild plant, which is thinner, more stunted and often marred by exposure to the sun, rain, and frost

On the basis of experimental and clinical studies, the root of *R Serpentina* is said to have the following pharmacological attributes (1) By action on the vaso-motor centre, it leads to generalized vaso-dilatation, with a lowering of blood pressure (2) By depressant action on the cerebral centres, it soothes the general nervous system (3) It exerts a sedative action on the gastric mucosa and a stimulating action on the plain musculature of the intestinal tract (4) It stimulates the bronchial musculature

A vague reference to the use of a tincture or alcoholic extract of the root of *R Serpentina*, in cases of high blood pressure, was made in 1942 by Paranjpe He claimed improvement, without any statistical backing, in most cases of hypertension, the hypotensive action was said to be particularly gratifying in elderly subjects and in the case of the diastolic pressure, the tincture was said to be a

good cough-sedative and diuretic   In two cases reported by Paranjpe, there had been a permanent reduction of blood pressure for well over a year, on occasional doses of the tincture

METHOD OF INVESTIGATION

Selection of patients   The fifty patients for investigation were selected from amongst a large number of cases of essential hypertension, who reported regularly at the clinic for treatment and who showed their willingness to co-operate   The diagnosis of essential hypertension was accepted on the basis of a routine clinical examination and investigations including urine analysis, ophthalmoscopic examination, orthodiagraphy, electrocardiography, and (in some cases) renal function tests and teleradiography   Only patients with systolic pressure over 160 and diastolic over 95 mm were admitted into this series   Cases of nephritic or renal hypertension, secondary hypertension, and malignant hypertension (diagnosed on the basis of clinical and ocular criteria) were rigidly excluded Of the 50 patients selected for study, 30 were males and 20 females, ranging in age from 39 to 76 years, the average age for the series being 59 years

Each patient was instructed to report for examination periodically, according to a rigid and pre-arranged plan   The routine adopted in each case was identical, viz   after an initial examination and check-up of the blood pressure (reading A), the patient was kept on a sedative capsule (containing 0 25 grains of prominal or phemitone) given three times daily for two weeks, the blood pressure being recorded again (reading B) and accepted as the actual " pre-treatment " level   This preparatory period of sedation exerts in my opinion a sort of stabilizing influence on the blood pressure of hypertensives, especially in those with hypersensitive nervous systems   Administration of *R Serpentina* tablets (one serpina tablet three times a day after meals) was then started, this dose being kept up for four weeks   The only other preparations permitted, during *R Serpentina* therapy, were laxatives, insulin injections (in diabetics), and occasionally tablets of aspirin for headaches   During serpina treatment, the blood pressure was checked and recorded once weekly (readings C, D, E, and F) In a few of my cases, the fall was so precipitate that further treatment had to be discontinued   After four weeks of serpina treatment, all medication was stopped for four weeks, during this interval or period of no treatment, the blood pressure was recorded twice, at fortnightly intervals (readings G and H)   A second course of serpina tablets (in the same doses) was then started and continued for

two weeks, at the end of this course, the blood pressure was recorded for the last time (reading J) The following nine sets of blood pressure readings were, therefore, recorded in each case   (A) at start of investigation, (B) after two weeks of sedative therapy, (C) after one week of serpina therapy (D) after two weeks of therapy, (E) after three weeks of therapy, (F) after four weeks of therapy (G) after a fortnight of no medication, (H) after four weeks of no medication, and (J) after two weeks of serpina treatment (second course)

The ritual observed at each check-up of the patient was properly standardized   At each attendance (arranged between the hours of 3 and 6 p m), the patient was made to rest in the waiting room for about half an hour   After a short history of symptoms and an enquiry for toxic reactions, the patient was subjected to a thorough clinical examination The blood pressure was recorded in the recumbent posture with the aid of a new Baumanometer, in accordance with the suggestions of the joint British and American Committees for standardization Of three consecutive readings at each sitting, only the third or last was accepted for recording purposes All the observations reported here were made by me using the same instrument throughout

In the present investigation, I have not concerned myself much with the improvement in individual symptoms, reported by patients, such a determination being liable to errors of interpretation In any case, the symptomatic status of such a case bears little or no relationship to the level of the blood pressure

In the presentation of results, all rises or falls of systolic blood pressure of less than 10 mm and of the diastolic of less than 5 mm have been classified as " insignificant," rises or falls of systolic pressure between 10 and 24 mm and of the diastolic between 5 and 14 mm as ' moderate ' and rises or falls of the systolic exceeding 25 mm and of the diastolic exceeding 15 mm have been classified as   marked

RESULTS OF INVESTIGATION

After two weeks of sedative therapy   After two weeks 28 of 50 patients showed a drop of systolic pressure ranging from 2 to 12 mm , the average fall being 6 mm   In 17 of the cases there was a rise ranging from 2 to 14 mm , with an average of 4 mm In the remaining 5 cases, there was no alteration at all   Taking all 50 cases into consideration   the average drop of systolic blood pressure after two weeks of sedation works out at under 2 mm

In the case of the diastolic blood pressure there was a fall in 30 cases ranging from 2 to 8 mm with an average of 3 mm , in 7 cases there wa

an actual rise ranging from 2 to 10 mm , with an average of 4 mm

AFTER ONE WEEK OF R SERPENTINA THERAPY

The immediate response of the blood pressure to *R Serpentina* therapy is shown in Table I

TABLE I

CHANGES OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE AFTER ONE WEEK OF R SERPENTINA THERAPY

Extent of alteration in blood pressure	Systolic blood pressure		Diastolic blood pressure	
	No of cases	Per cent	No of cases	Per cent
From +10 to +6 mm	1	2	1	2
+5 to +1 mm	8	17	8	17
No change—	2	4	4	8
−1 to −4 mm	7	15	18	38
−5 to −9 mm	11	23	12	25
−10 to −14 mm	7	15	4	8
−15 to −19 mm	2	4	1	2
−20 to −24 mm	5	10	0	0
−25 to −29 mm	2	4	0	0
−30 to −34 mm	2	4	0	0
−35 to −40 mm	1	2	0	0
From +10 to −40 mm	48	100	48	100

Systolic blood pressure Of the 48 cases studied (two of our patients having absented themselves), as many as 37 cases showed a drop of systolic pressure, ranging from 2 to 38 mm with an average drop of 13 mm In 2 cases it remained unaltered whilst in 9 there was actually a paradoxical rise, ranging from 2 to 6 mm with an average rise of 3 mm

A " moderate " fall (i e 10 to 24 mm) was noted in 14 out of 48 cases and a " marked " fall (i e 25 mm or over) in 5 cases In other words, of my 48 cases, 19 cases (or 39 5 per cent) showed a response within a week of commencement of serpina treatment

Diastolic blood pressure Of the 48 cases, 35 showed a fall of diastolic pressure ranging from 2 to 18 mm , with an average of 6 mm , in 4 cases the diastolic level remained unaffected whilst in 9 there was an actual rise ranging from 2 to 6 mm with an average of 3 mm

The diastolic fall was classified as being of " moderate " degree (i e 5 to 14 mm) in 16 cases and as " marked " (i e 15 mm or over) in 1 case A good result (i e a diastolic drop of 5 mm or more) was therefore obtained in 17 cases (See Table I)

2B

In 35 of my 48 cases, there was a drop of both systolic and diastolic pressure, after one week of drug treatment, in 6 cases there was a paradoxical rise of both systolic and diastolic pressure whilst in the remaining 6 cases there was a rise of one with a fall of the other

AFTER FOUR WEEKS OF R SERPENTINA THERAPY

The delayed response of the blood pressure to drug therapy is given in Table II

TABLE II

CHANGES OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE AFTER FOUR WEEKS OF R SERPENTINA THERAPY

Extent of alteration in blood pressure	Systolic blood pressure		Diastolic blood pressure	
	No of cases	Per cent	No of cases	Per cent
From +20 to +11 mm	1	2	0	0
+10 to +1 mm	6	13	6	13
No change—	0	0	3	7
−1 to −9 mm	5	11	17	36
−10 to −19 mm	14	30	18	38
−20 to −29 mm	9	19	2	4
−30 to −39 mm	10	21	1	2
−40 to −49 mm	1	2	0	0
−50 to −60 mm	1	2	0	0
From −20 to −60 mm	47	100	47	100

Systolic blood pressure Of the 47 cases studied (three failed to report for check-up), as many as 40 responded to serpina therapy by showing a drop of systolic pressure, ranging from 2 to 54 mm with an average of 21 mm A rise of 4 to 12 mm , with an average of 6 mm was noted in the remaining 7 Taking all the cases into consideration, the average fall worked out at 19 mm , with a range of +12 to −54 mm

The systolic fall was described as being " moderate " in 22 cases out of 47 and as " marked " in 13 cases In other words, a good systolic response (i e 10 mm or over) was noted in 35 of 47 cases, after four weeks of serpina therapy

Diastolic blood pressure In 38 out of the 47 cases there was a drop of diastolic pressure ranging from 4 to 34 mm , with an average of 11 mm , in 3 cases, the diastolic level remained unaltered whilst in 6 cases there was an actual rise varying between 2 and 10 mm , the average being 5 mm Taking all cases into consideration, the diastolic pressure showed an average drop of 10 mm , the range of variation being from +10 to −34 mm

The diastolic fall, after four weeks of therapy, could be classified as "moderate" in 27 of the 47 cases and as "marked" in 7 cases A good diastolic response (i e 5 mm or over) was therefore obtained in as many as 34 out of 47 cases

In as many as 29 of my 47 cases there was a "moderate" or "marked" fall of both systolic and diastolic pressures, in 6 cases such improvement was confined to systolic levels only, and in 2 to the diastolic levels only

Types of blood pressure response, during R Serpentina therapy According to the rapidity and degree of fall of the systolic blood pressure during drug treatment, I have been able to recognize five main types of blood pressure curves   (1) A gradual fall continued throughout the course of treatment (21 of my 50 cases)   (2) The plateau type, where the systolic level showed little or no alteration throughout treatment (12 cases)   (3) A precipitate initial drop with a gradual decline subsequently (8 cases)   (4) An initial plateau with subsequently, a gradual decline (5 cases)   (5) A precipitate initial drop with subsequently a plateau (3 cases)

From the behaviour of the pressure (especially systolic), a graph can easily be constructed to determine the type of response to drug treatment, in any given case

AFTER CESSATION OF R SERPENTINA THERAPY

These studies were undertaken with a view to determine whether the hypotensive action of serpina is strictly limited to the period of its administration or whether it is continued for some time after

After two weeks The persistence of the hypotensive action of R Serpentina was studied in the 41 cases in my series, who had responded to its administration by a fall of blood pressure, unfortunately, 5 of these having failed to report for their periodical check-up, our enquiry has had to be limited to a total of 36 cases Two weeks after stoppage of serpina treatment, the results were as follows In 22 of the 36 cases the low levels induced by serpina tablets were well maintained, in 8 cases they were partially maintained, in 3 cases they had returned to their levels of before treatment, in the remaining 3 cases there was a further fall

After four weeks Thirty-nine cases could be investigated from this point of view The results were as follows In 10 the low levels were well maintained, in 15 cases they were partially maintained, in 10 cases they had returned to the level before treatment, in 4 cases the pressure showed a further drop The hypotensive action of R Serpentina was, therefore, perceptible in 91 per cent

of my cases for two weeks and in 74 per cent for four weeks after discontinuance of the drug

AFTER A SECOND COURSE OF R SERPENTINA

In order to test the drug for consistency of action, all the 50 cases of my series were subjected to a second course of serpina tablets after an interval of four weeks The tablets were administered in the same doses, but for two weeks only The results of this second course were most satisfactory, making allowance for the fact that as many as 36 per cent of the cases were still under the hypotensive influence of the first course of tablets The average drop of systolic blood pressure after the first course had worked out at 17 mm , the maximum fall recorded in any case being 44 mm   In the case of the diastolic pressure, the corresponding values worked out at 7 mm and 22 mm respectively

After two weeks of the second course, the average systolic fall worked out at 10 mm , the maximum drop in any case being 24 mm   The corresponding values for the diastolic pressure were 5 mm and 12 mm respectively

The blood pressure behaviour after the second course of tablets was very similar to that after the first, in the great majority of the cases However, in one case there was a drop of pressure during the first course but a rise during the second, the reverse happened in one case

TOXIC EFFECTS AND REACTIONS FROM R SERPENTINA

After having used the dried root of *R Serpentina* in several thousand cases of high blood pressure, both in hospital and private practice, I can vouch for the non-toxicity of the drug with confidence, I have, so far, not come across a single fatality from the administration of this preparation Even when the administration has been continued without a break for as long as two to five years (as in some of my cases), and even in the presence of cardiac or renal complications, there have been no ill-effects of a serious disabling or permanent nature

The following reactions were reported by some of my cases, during the present investigation

Excessive drowsiness or sleepiness	6 cases
Feeling of depression or lassitude	4 cases
Diarrhœa	3 cases
Anorexia	2 cases
Nausea and vomiting	2 cases
Vertigo or giddiness	2 cases
Increase of polyuria and nocturia	2 cases
Abdominal griping pain	1 case

The commonest disturbance after *R Serpentina* administration, in my experience, has been that of

excessive drowsiness or sleep, to some of the hypertensives suffering from insomnia, this may prove a blessing in disguise Diarrhoea is usually of a mild order and responds readily to treatment On the whole, *R Serpentina* preparations are very well tolerated by patients and appear non-toxic in therapeutic doses The only contra-indications, in my opinion, are severe or intractable diarrhoeas or dysenteries and cases of hypertension of renal or malignant type, where this form of treatment proves of no avail

At the present time, *R Serpentina* preparations, as manufactured in India, have one serious drawback to their use, not being properly standardized or assayed, the hypotensive action of the drug is not strictly constant from batch to batch of the drug. For some time now, the physicians of this country have felt the need for a more satisfactory and standard preparation of this drug, the action of which can be predicted at all times

SUMMARY AND CONCLUSIONS

The hypotensive action of *Rauwolfia Serpentina* (N O *Apocynacæ*) has been subjected to clinical trial in a series of fifty cases of essential benign hypertension Tablets of the dried root of this plant were prescribed in optimum doses, the patients being subjected to periodical check-ups of the blood pressure, according to a pre-arranged plan

Within a week of *R Serpentina* therapy, 77 per cent of my cases showed a drop of systolic blood pressure ranging from 2 to 38 mm , with an average drop of 13 mm A drop of 10 mm or over was noted in 40 per cent of cases

In the case of the diastolic blood pressure, 73 per cent of cases displayed a drop ranging from 2 to 18 mm , with an average drop of 6 mm , a diastolic response of 5 mm or over was noted in 35 per cent In 73 per cent of cases, there was a drop of both systolic and diastolic blood pressure after one week of therapy

After four weeks of *R Serpentina* therapy,

85 per cent of cases displayed a drop of systolic blood pressure varying from 2 to 54 mm with an average of 21 mm A systolic drop of 10 mm or over was noted in as many as 74 per cent of cases

In 81 per cent of cases, the diastolic pressure showed a drop of 4 to 34 mm with an average of 11 mm A diastolic fall of 5 mm or over was noted in 72 per cent

In 62 per cent of cases there was a " moderate " or " marked " drop of both systolic and diastolic pressure levels

According to the behaviour of the blood pressure, I was able to recognize five types of response to *R Serpentina* therapy, which have been described

The hypotensive action was apparent in 91 per cent of cases two weeks after stoppage of all treatment and in 74 per cent even after four weeks of no treatment

A second course, of two weeks, was tried in all the cases after an interval of four weeks, the blood pressure response to the second course of tablets was almost as good as during the first

R Serpentina appears to be a perfectly safe remedy, devoid of any serious or toxic ill-effects Amongst the few unpleasant symptoms encountered during its administration, were excessive drowsiness (in 12 per cent), lassitude (in 8 per cent), diarrhoea (in 6 per cent), anorexia (in 4 per cent) and nausea with vomiting (in 4 per cent)

On the whole, the results of *R Serpentina* therapy, in the present series, have been most encouraging In most cases it was proved capable of lowering both systolic and diastolic blood pressure Although its action is temporary in many cases, it can be reproduced successfully by a second administration of the drug No serious reactions to therapy were encountered in any of the cases *R Serpentina*, therefore, satisfies all the criteria of a successful hypotensive agent formulated by Evans and Loughnan (1939) Judging from the results of the present investigation, it has a definite place in the treatment of cases of high blood pressure

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THE PHONOCARDIOGRAPHY OF HEART MURMURS

PART I—APPARATUS AND TECHNIQUE

BY

E D H COWEN AND D H PARNUM

From the Department of Medicine, Cambridge University, and the Cambridge Instrument Company

It was considered important to subject the points made by William Evans (1947) to further examination by phonocardiography We hoped to define the sphere of usefulness of this instrument in aiding the clinician in the diagnosis of patients presenting with murmurs of the heart

The Cambridge Instrument Company kindly supplied a standard phonocardiograph outfit in every way similar to that used by Evans It was decided to attempt a rough estimate of the suitability of this instrument by taking gross clinical examples of organic heart disease and subjecting them to phonocardiography, since it was considered axiomatic that the instrument must be able to record all the murmurs that could be heard on simple clinical auscultation It was soon found that the standard instrument was incapable of recording the majority of relatively high pitched systolic and diastolic murmurs

The Research Department of the Cambridge Instrument Company then kindly agreed to develop a modern apparatus from the new physical data that have been made available over the last twenty years, it was agreed that the clinical and scientific aspects should be closely co-ordinated The apparatus is described later

Those concerned with the visual recording of the heart sound vibrations must be grateful for the work of Rappaport and Sprague (1941 and 1942) in amplifying the basic data on which a reliable phonocardiograph should be constructed

The heart sound vibrations are modified by the thoracic tissues as they radiate to the chest wall This distortion will vary from person to person and is probably dependent largely on the amount of adipose tissue of the thoracic organs and of the chest wall itself and must remain an indeterminate variable in clinical phonocardiography

Once the heart sound vibrations have reached the chest wall they are further modified for a clinician listening to the sounds with a stethoscope by the stethoscope, which produces a certain degree of attenuation of sounds of low frequency, and by the human ear, which in the auscultatory range has a practically logarithmic low frequency attenuation response (see Fig 2)

There are therefore three phonocardiographic records that may be considered physiological

(1) A linear phonocardiogram This is a visual record of the heart sound vibrations as they occur at the chest wall without any modification other than undistorted amplification, hence the term linear The heart sound vibrations consist of an intense low frequency component (palpable but not audible) and a faint higher frequency component (audible) The linear phonocardiogram, however, resembles a jugular venous pulse record for it only shows the intense low frequency component This component is 100,000 to 1,000,000 times more intense than the higher frequency vibrations which consequently cannot be shown on the same scale (see Fig 9A and B, 11A and B, Part II)

(2) A stethoscopic phonocardiogram This is a visual record of the heart sound vibrations from the chest wall as modified by an average stethoscope, that is as presented to the human ear Such records will show low frequency events such as the third and fourth heart sounds as well as the whole range of murmurs and are the most generally useful phonocardiograms (see Fig 4–8 and 10A and B, Part II)

(3) A logarithmic phonocardiogram This is a visual record of (2) above, plus the additional modification of the average normal human ear In other words it is a visual representation of the vibrations as presented to the sensorium of a listening clinician The advantages of this type of record are firstly that its amplitude corresponds to the loudness heard by the clinician (a sound heard twice

as loud as another sound will be twice the amplitude of the other on the record), and secondly that as the low frequencies are extremely attenuated, a record taken from a patient with heart murmurs may be easier to interpret than one in which low frequency events are also recorded   Such a record should therefore be used to add to the information of a stethoscopic tracing (see Fig 3, 9B, 10C, 11A and B, Part II)

It is necessary to record simultaneously some other manifestation of cardiac activity to provide a reference tracing for interpreting the phonocardiogram   The following tracings have been used for this purpose—the electrocardiogram, the subclavian or jugular venous pulse, the apex beat cardiogram and in special cases the arterial pulses

The electrocardiogram has been used extensively because it can be recorded easily, but the only reliable reference point it gives is that mechanical ventricular systole never precedes the QRS complex of the electrocardiogram

Since the electrocardiogram gives no reference points in diastole it is misleading to use it to determine the phase of the cardiac cycle of any diastolic event, either sounds or murmurs (see Fig 5), it is, however, a valuable additional reference tracing to an apex beat or venous pulse recording, particularly when auriculo-ventricular dissociation is present or when there is some abnormality of propagation of the cardio-excitatory impulse

The subclavian or jugular venous pulse gives, in addition to the onset of ventricular systole, the onset of auricular systole, the beginning of the second sound and a fair indication of the site of the third heart sound

The apex beat tracing (linear phonocardiogram) gives the onset of ventricular systole, the beginning of the second sound and the third heart sound, it is as a rule easier to record by electrical means than the venous pulse and requires no time correction for vessel transmission of vibrations as does the venous pulse

The heart sounds and most murmurs are noises in acoustic terminology, which means they are conglomerations of sound vibrations of various frequencies harmonically unrelated   In some cases, therefore, it is impossible to determine the exact onset of a murmur that follows a heart sound   Moreover, there is some variation in the vibrations recorded from one heart cycle to the next

THE PHONOCARDIOGRAPH

The apparatus used consists of a crystal microphone, a two-stage valve amplifier, and a Cambridge double string Einthoven galvanometer   One fibre of this galvanometer is used for the electrocardiogram in the normal way, the other, which is used for the phonocardiogram, is tightened to its full extent in order to raise its high-frequency response   In this condition its sensitivity is about 1 mV/mm

From examination of our phonocardiograms it will be noted that large excursions of the phonocardiographic fibre displace the electrocardiographic fibre   It has been proved experimentally that this is an air pressure phenomenon and not an electromagnetic interference, and that the phonocardiographic fibre is not affected by large excursions of the electrocardiographic fibre   The explanation of this effect lies in the greater sensitivity of the loose electrocardiographic fibre when it is calibrated for clinical use

The microphone used is a Cosmocord Mic-6   This microphone was originally chosen because of its high sensitivity and high internal capacity   It has the disadvantage of being nearly 2 inches in diameter, so that good contact between the microphone and the chest is not always easy to attain   The sensitivity is stated by the makers to be about 10 mV/dyne/sq cm in the phonocardiographic frequency range

The microphone is placed in a brass case which forms the chest piece   A ring of sorbo rubber is cemented to the case to assure good contact with a chest wall of irregular contour   The volume of the air chamber coupling the chest wall to the diaphragm is about 14 ml   The case is not intended to have any selective frequency properties, the intention is that the microphone and amplifier should have a fundamentally flat response, any other type of response being produced by controllable electrical filters in the amplifier

The amplifier circuit is shown in Fig 1   As the output has only to operate a string galvanometer the gain is not high, the voltage gain from the input to the galvanometer terminals being 100   A switched attenuator, placed between the two stages, controls the gain in steps of 2 1, and a universal shunt connected across the galvanometer gives continuous control of gain at any setting of the attenuator   In phonocardiography, calibration of the controls is of little value, but they must cover a very wide range in order to deal with the varying *levels of heart sound vibrations encountered*

In order to make the fundamental response as flat as possible, a 10-megohm resistor is placed across the microphone, which has a capacity of 0 002 μF   This gives a time constant of 0 02 second which, since it is the shortest time constant in the whole system, will control the low-frequency response, it should result in the response being down to half at about 8 c/cs   As explained later, such a response was not obtained
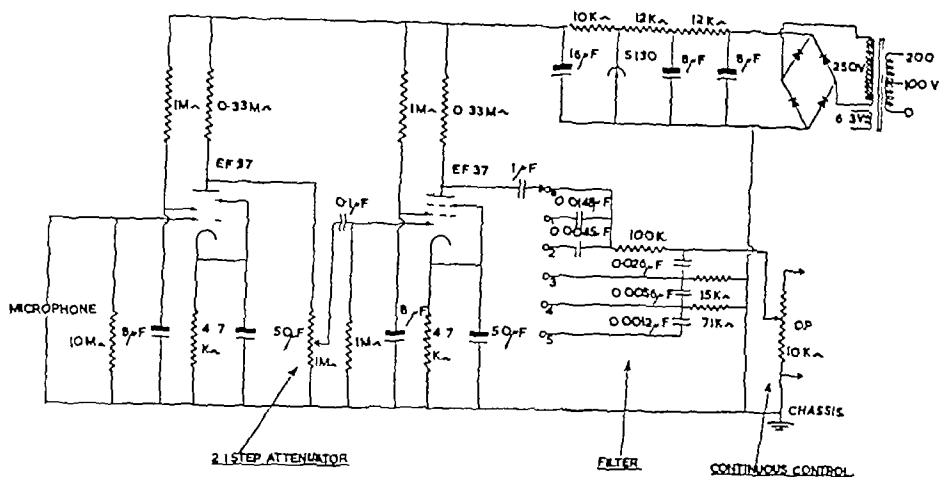
FIG 1 —Amplifier circuit of phonocardiograph

A 6-position filter, controlling the low-frequency response, is placed between the output stage and the galvanometer At setting 0 the amplifier response is flat At settings 1, 2 and 3 single-stage condenser-resistance filters, giving time *constants of 0 0064, 0 002 and 0 0004* seconds respectively, are provided These values give a loss of 3 db at 25, 80 and 400 c/s respectively, and a loss approaching 6 db/octave below these frequencies (stethoscopic phonocardio gram settings)

At settings 4 and 5, a 2-stage and 3-stage filter respectively are introduced, the time-constant of each additional section being 0 0004 seconds These filters begin to cut off between 400 and 500 c/s (like that of setting 3) and give a loss approaching 12 and 18 db/octave respectively below these frequencies (logarithmic phonocardiogram settings)

Fig 2 shows measured frequency responses for the assembly of microphone, amplifier, and galvano-meter These results were obtained by applying a variable frequency sound stimulus to the micro-phone with a pistonphone calibrator Two points require comment First, the low-frequency re-sponse at setting 0 is not flat, this is the result of accoustic leakage in the microphone assembly The chief cause of this leakage is a felt ring which the makers fit round the rim of the microphone case It is proposed in future to work without this ring, so that the response can be entirely controlled by the electrical circuit Secondly, the response begins to fall above 500 c/s This is the result of the galvano-meter properties The microphone has a resonance at about 2500 c/s, but the low galvanometer response at this frequency entirely masks this resonance

The high-frequency response attained is probably sufficient for the purposes of phonocardiography

Conventional mains power supplies are provided Rough HT stabilization is obtained by an S 130 gas tube, and the valve heaters are run on a c HT variations and heater pick-up are not unduly troublesome, but improvements in both these respects are desirable

Special cable, type K 16 G M made by Telegraph Construction and Maintenance Co Ltd , is used for the microphone input lead This gives a very considerable reduction in the extraneous voltages produced when the microphone cable is moved in any way

The advantages of a string galvanometer over other methods of recording high frequency pheno-mena are not great when an amplifier is essential It was used in the research detailed in Part II because it was available Comparative experiments have therefore been made with a double Duddell oscil lograph, which has a wider frequency range and is more robust This instrument, used in con junction with appropriate amplifier circuits and a smaller microphone free from acoustic leakage, has been tried with promising results, Fig 9A and B, 11A and B, Part II were taken with such an apparatus The addition of an electrocardiographic channel is under consideration, but the whole of the apparatus is regarded as purely experimental at the moment

The tracings are photographed at a speed which facilitates the accurate reading of phonocardio-grams

(References will be found at the end of Part II)
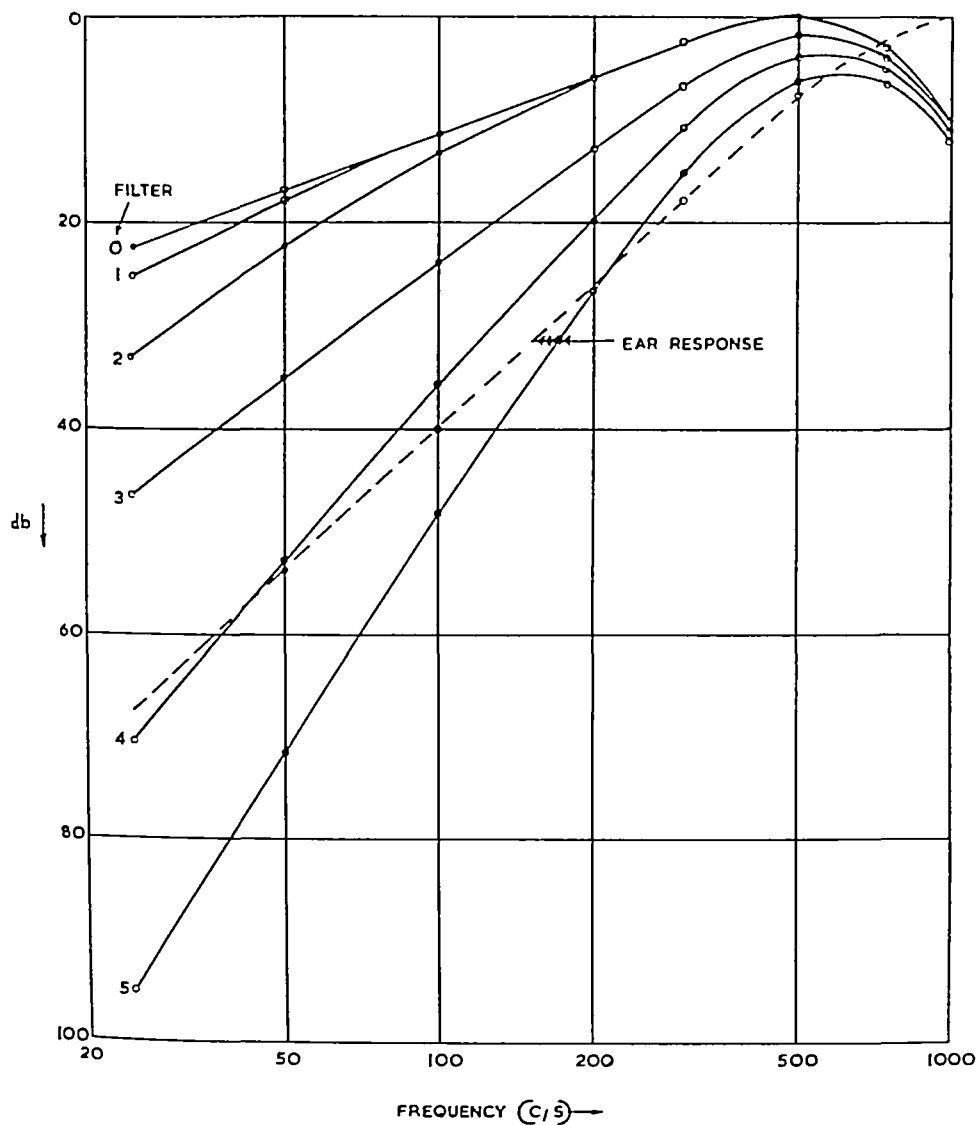
FIG 2.—Frequency response curves of phonocardiograph and of " normal " human ear (audiogram)

THE PHONOCARDIOGRAPHY OF HEART MURMURS
Part II—Clinical Results and Discussion

BY

E D H COWEN

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Papers by William Evans (1947) suggested that the phonocardiograph could aid the clinician in the elucidation of the following points (1) the distinction between the systolic murmur found with organic heart disease and the systolic murmur found with no organic heart disease, referred to as an innocent murmur, (2) the murmurs found in mitral stenosis, (3) the distinction between aortic incompetence of rheumatic as opposed to that of syphilitic ætiology, and (4) the presence of unsuspected aortic diastolic murmurs in cases of hypertension

SYSTOLIC MURMURS

One important problem in clinical cardiology is the investigation of systolic murmurs in the hope that the healthy youngster with a systolic murmur can be saved from some form of cardiac invalidism imposed by the medical profession

Evans (1947) found that the systolic murmurs in organic heart disease, with the exception of those found in hypertension, heart block, and a few cases of aortic valvular disease if recorded from the mitral area (which are all unimportant from the above standpoint), occur early in electrical systole, whereas the systolic murmurs recorded in subjects without clinical heart disease—the "innocent" group—occur in mid or late electrical systole

Evans used the S line, a line drawn through the end of the S wave of lead II of the electrocardiogram to touch the simultaneously recorded phonocardiogram to distinguish the two groups A systolic murmur occurring at the S line was found in the organic group while a systolic murmur beginning some distance after the S line was found in the innocent group In none of the innocent group was a diastolic murmur recorded

To investigate this point two series of cases were collected clinically and checked by cardioscopy and electrocardiography

Group I consisted of 57 cases of known congenital or valvular heart disease with systolic murmurs to auscultation and phonocardiography (see Fig 3-6, 8A, B, and C, 10A, B, and C)

Group II consisted of 27 cases with obvious systolic murmurs but with no other evidence of disease An obvious systolic murmur has been taken as one lasting an appreciable interval into systole between the first and second heart sounds and of not less than moderate intensity (Grade III, Levine, 1945), for it is this group of murmurs that presents a clinical difficulty as to whether organic disease is present or not In four cases the systolic murmur was loud or very loud (Grade IV or V) and one of these suffered an undoubted attack of subacute bacterial endocarditis after the investigation—emphasizing that an organic lesion was present although careful cardiological investigation revealed no deviation from the normal other than a loud systolic murmur Twenty one of these cases (77 per cent) were aged 30 or under (See Fig 7A, B, and C)

The phonocardiograph employed recorded a stethoscopic or logarithmic phonocardiogram with lead II electrocardiogram as reference tracing (See Part I) The time-marker on all the records is 0 2 seconds Records are marked to show the

TABLE I

RELATION OF ONSET OF SYSTOLIC MURMURS TO S LINE IN LEAD II ELECTROCARDIOGRAM

Timing	Valvular or congenital heart disease 57 cases		No diagnosed heart disease 27 cases	
After S	38	66 6%	27	100%
At S	9	15 7%	—	—
Doubtful	10	17 5%	—	—
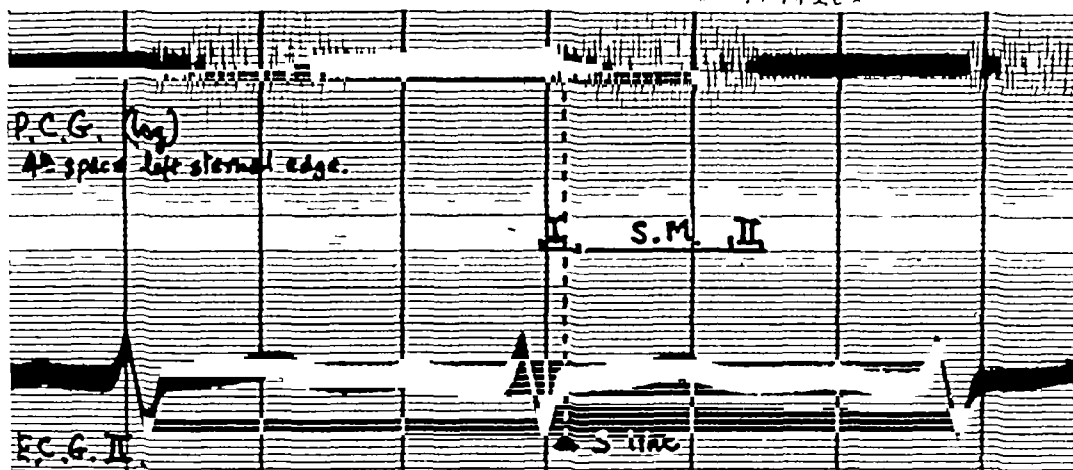
FIG 3 —Ventricular Septal Defect   Logarithmic phonocardiogram from site of maximal intensity of murmur—note that low frequencies in the first and second heart sounds are not recorded, and that the base line is very clear
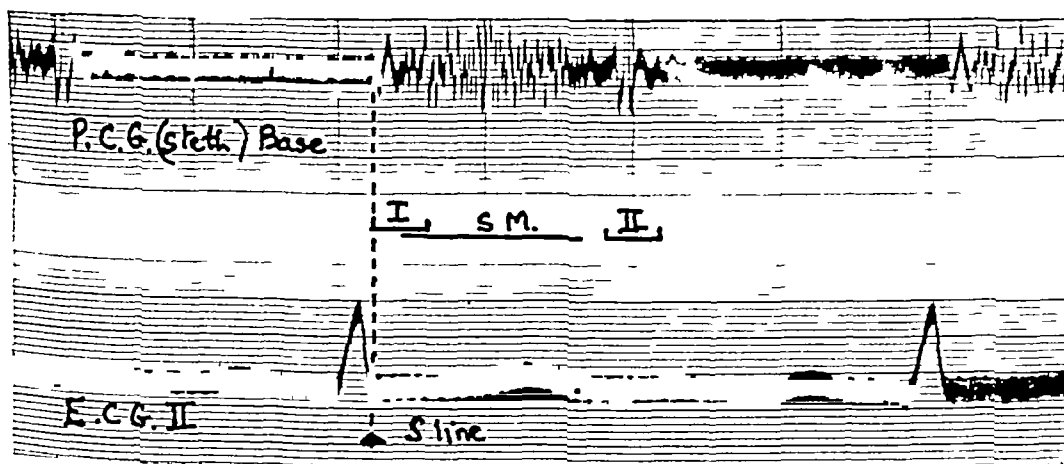
FIG 4 —Aortic stenosis   A second heart sound was audible at the base and is recorded

S line, the heart sounds I, II, III, and IV, systolic murmurs (S M), and diastolic murmurs (D M) Other lettering is explained under the appropriate figure   The site from which the record has been taken is indicated after the type of phonocardiogram shown (steth = stethoscopic, log = logarithmic)

It will be seen that in two-thirds of the organic cases the systolic murmur began after the S line, whereas only in 9 did it begin at the S line   A further analysis (Table II) of these 9 cases shows that a systolic murmur occurring at the S line can occur with most forms of valvular or congenital heart disease but wherever there were sufficient

cases to draw any conclusions it appears to be uncommon in any particular defect   (See Fig 8A)

It would appear from this investigation that the systolic murmurs encountered in valvular and congenital heart disease cannot be differentiated from the systolic murmurs occurring with no recognizable heart disease by their relation to the S line of lead II of the electrocardiogram   For although in all the Group II cases the systolic murmur occurred after the S line, the same applied to at least 66 per cent of the cases in Group I

It has been known for many years that mechanical and electrical systole in man and experimental
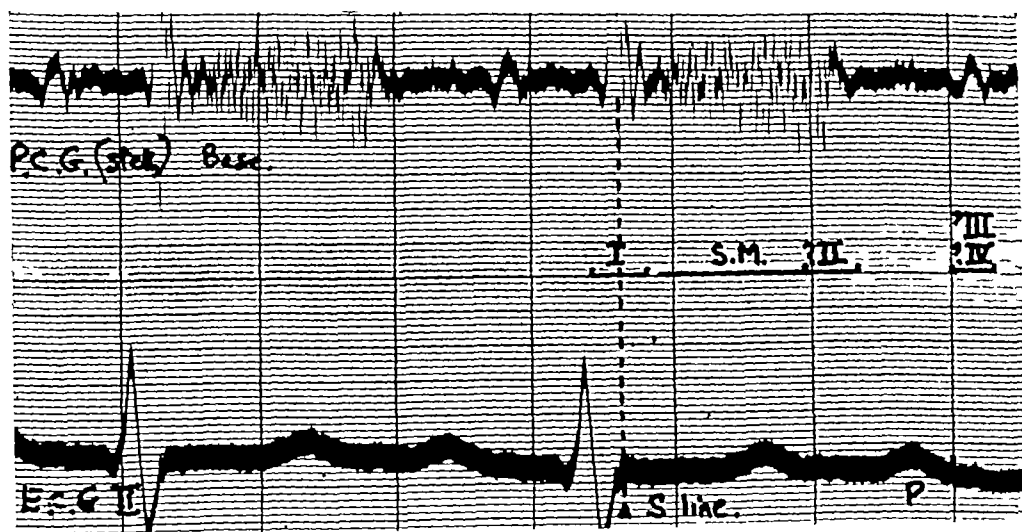
FIG 5 —Pulmonary stenosis   No second heart sound was audible or is recorded   Record shows a low frequency event marked ?III ?IV which could be either a third heart sound because it occurs about 0 2 sec after the second heart sound, or a fourth heart sound occurring as it does just after the P wave of the electrocardiogram, or a combination of both   The electrocardiogram cannot be used to differentiate these possibilities

TABLE II

ANALYSIS OF RELATION OF ONSET OF THE SYSTOLIC MURMUR TO THE CLINICAL DIAGNOSIS IN ORGANIC HEART DISEASE

Diagnosis	Site of record	No of cases with S M at S line	No of cases with S M after S line	No of cases with doubt-ful on-set of S M
Aortic incompetence	Base	3	12	3
Aortic stenosis	Base	1	1	0
Mitral stenosis	Apex	1	11	2
Combined rheumatic valvular lesions	Apex	1	5	2
Active rheumatic carditis	Apex	1	0	0
Auricular septal defect	Base	1	0	2
Ventricular septal defect	4th space left sternal edge	1	2	1
Pulmonary stenosis	Base	0	3	0
Fallot's tetralogy	Apex	0	2	0
Patent ductus arte riosus	Base	0	1	0
Lutembacher s syn drome	Apex	0	1	0
Total		57	9	38	10

animals are not simultaneous either in onset or in duration (Wiggers, 1944)   Such asynchrony would provide the simplest explanation for the varying relation of systolic murmurs to the S line of the electrocardiogram   Thus in Fig 4 the whole of the first heart sound occurs after the S line

It will also be noted that it is a condition of the cases in Group II that they should have a normal electrocardiogram, whereas many cases in Group I had abnormal electrocardiograms often with a widened QRS interval   However, only 3 of the 9 cases with a systolic murmur at the S line had a widened QRS interval

MITRAL STENOSIS

Evans (1947) found that when a systolic murmur was heard without a presystolic murmur in mitral stenosis, the murmur as recorded by phonocardiography started during the P-R period of lead II of the electrocardiogram in 33 out of 41 cases   In other words the murmur was really presystolic and not systolic in timing and due to auricular contraction   He also found that the systolic murmur never occurred later than the S line and that there was a mid diastolic murmur in all of his 74 cases

To test these points a consecutive series of 30 cases of mitral stenosis was investigated   (See Fig 8A B, and C)   In 17 of these cases a systolic murmur was recorded as it was heard   It never occurred

FIG 6—Atrial septal defect   Note splitting of the first and second heart sounds   This is not a good record as it shows   mush '

during the P–R period of the electrocardiogram In all 17 it occurred after the first heart sound   Its relation to the S line lead II electrocardiogram was as follows

After the S line in	12
At the S line in	2
Exact onset doubtful in	3

In 15 of the series a presystolic murmur was heard, and in all 15 cases it was clearly seen on the record during the P–R period of the electrocardiogram   It was always separate from a systolic murmur if present and also differed from such a systolic murmur in that its mean frequency was considerably lower (See Fig 8C)

The position of the second heart sound in Fig 8A and B has been determined by taking phonocardiographic records from the base of the heart where the second sound was clearly seen in these cases and transposing to the apical records   Apical and basal records were taken within a few minutes of one another   (Fig 10A is a record from the base of the heart and Fig 8A an apical record in a case of combined mitral stenosis and aortic incompetence)   The second heart sound is probably split in Fig 8C

It is my impression that the sole information which the phonocardiograph has added to that of auscultation in the cases of mitral stenosis in this series is that a mitral diastolic murmur occurs more frequently than it is heard   However, one cannot be certain of this unless the record shows a clear base line, and this was not always obtained

Problems such as whether an opening snap of the mitral valve is always present in mitral stenosis, and the differentiation of this snap from a third heart sound (which may be of diagnostic importance in mitral stenosis) could not be investigated owing to the limitations imposed by the apparatus in having no other reference tracing than the electrocardiogram   Fig 9A is an apical record from a case of mitral stenosis, with a linear phonocardiogram (apex cardiogram) as reference tracing in which a third heart sound is clearly indicated and in which no opening snap of the mitral valve is shown

AORTIC INCOMPETENCE

Evans, in a series of 20 cases of aortic incompetence, found that 8 were clinically of syphilitic ætiology and 12 of probable rheumatic origin, although with no definite evidence of this after full cardiological investigation   After phonocardiography at the apex he considered that there was proof of rheumatic ætiology in 16 out of the 20 cases because of the presence of presystolic and mid-diastolic murmurs from added mitral stenosis

To test this finding a series of 21 consecutive cases of aortic incompetence was investigated clinically (see Fig 10A, B, and C), 11 were considered to be of rheumatic, 5 of syphilitic, and 5 of unknown ætiology

Of the 11 rheumatic cases, 5 had definite evidence of mitral stenosis both to clinical and to phono-cardiographic examination (See Fig 10A and 8A taken from same patient)   In the remaining 6
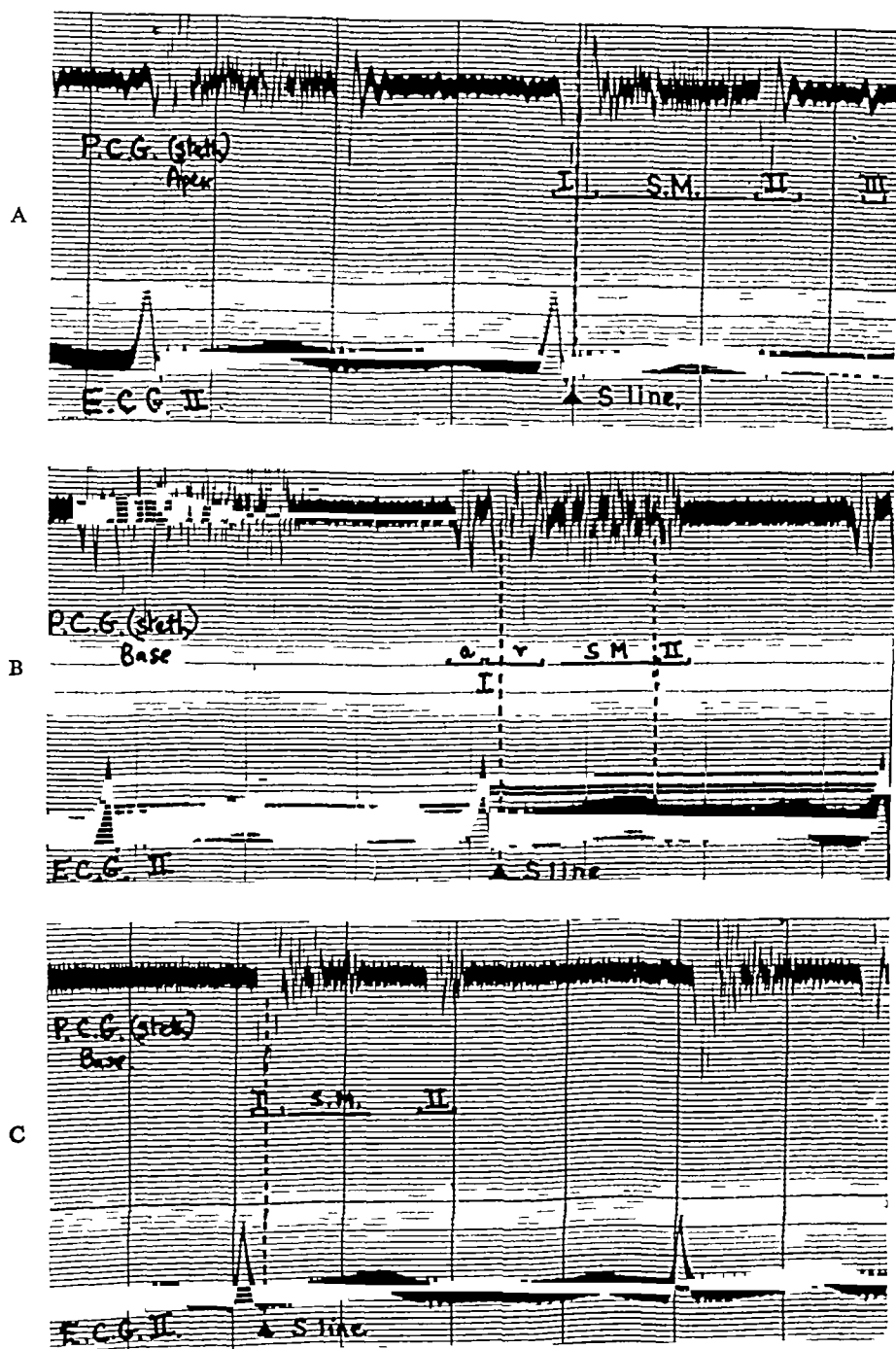
FIG 7—"Innocent' systolic murmurs   Note that the relation of the systolic murmur to the S
line does not differ from that found in organic heart disease
In (B), note the auricular part of the first heart sound (a)
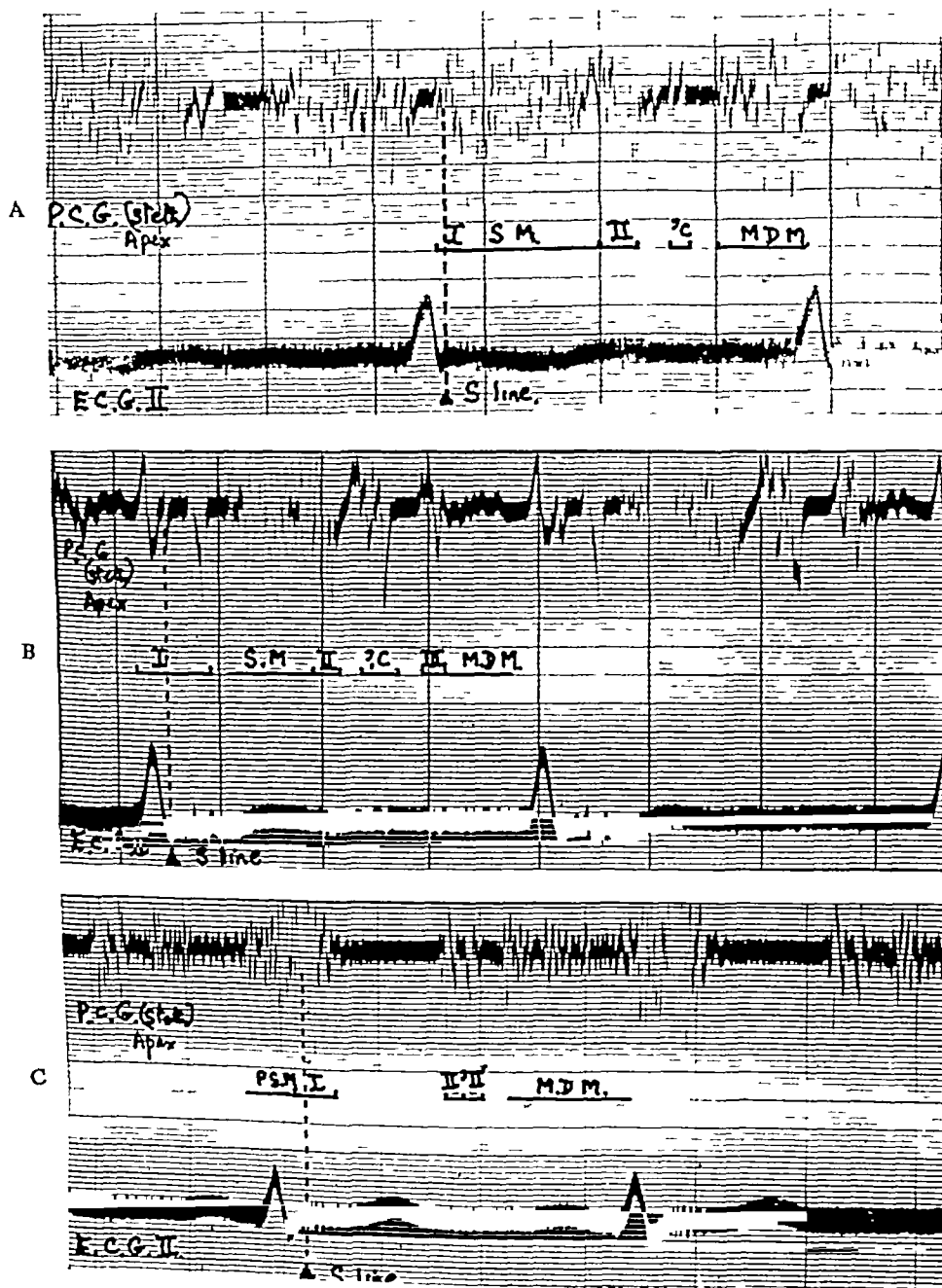
FIG 8 —Mitral stenosis—apical recordings   Three patients
(A) Systolic murmur (S M) starting at the S line
(B) Systolic murmur starting well after the S line
(C) No systolic murmur
A presystolic murmur (P S M) is only shown in (C), auricular fibrillation being present in (A)
and (B)
The opening snap of the mitral valve is probably shown at (c) in (A)   Mid-diastolic murmur
(M D M)
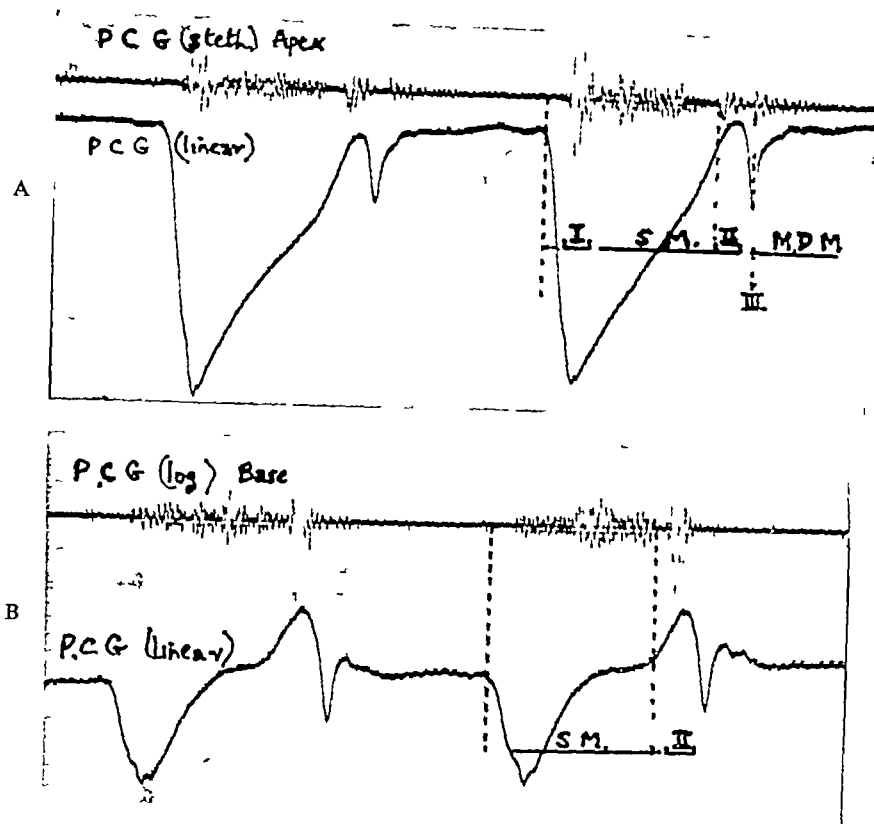
Fig 9 —Mitral stenosis   (A) Apical and (B) basal records of one patient   A loud pulmonary second sound was heard and the large amplitude of this sound in the logarithmic basal record is well seen

cases there was no auscultatory or phonocardiographic evidence of mitral stenosis, although in 2 of these the apical records showed long aortic diastolic murmurs that might have obscured any mitral mid-diastolic murmurs present

Of the remaining 10 cases in the series, none showed phonocardiographic evidence of mitral stenosis although 4 had long aortic diastolic murmurs recorded on the apical records, which might have obscured any mitral mid diastolic murmurs present

One case with aortic incompetence and subacute bacterial endocarditis, but of uncertain aetiology, in which no evidence of mitral stenosis had been heard or recorded by phonocardiography, died Post-mortem, no enlargement of the left auricle was found, there was no evidence of rheumatic endocarditis or valvulitis, and microscopy did not elucidate the aetiological diagnosis

In this series of cases of aortic incompetence no additional information to that found on clinical examination was given by phonocardiography

UNSUSPECTED AORTIC DIASTOLIC MURMURS IN HYPERTENSION

Evans found aortic diastolic murmurs in 12 of a series of 43 hypertensive cases and in some cases of heart block   In order to test this finding a series of 20 cases of hypertension with loud or ringing aortic second sounds and diastolic blood pressures con sistently over 100 mm was investigated   In no case was a diastolic murmur heard clinically   The ringing quality as heard by auscultation showed itself as a musical second sound of no greater width than normal on phonocardiographic records taken from the aortic area, and no diastolic murmur was detected after the second sound in any case (See Fig 11A and B)

Evans in interpreting his records has stated that " at the end of the T wave (lead II electrocardiogram) the second sound starts   Such a relationship has not been observed by other users of the phonocardiogram (Orias and Braun-Menendez, 1939)   It can be seen from Fig 7B and 10B that
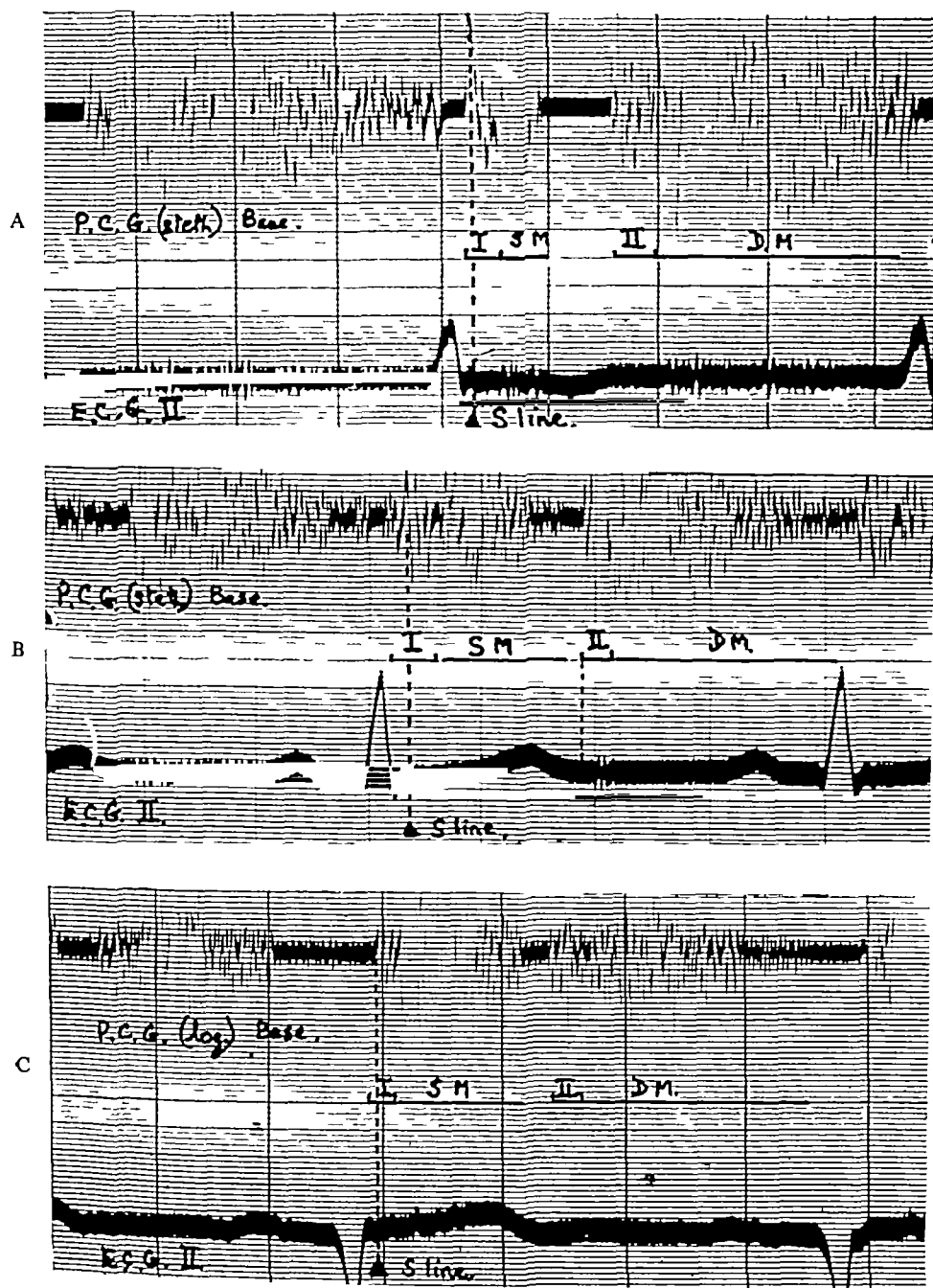
FIG 10.—Aortic incompetence—basal recordings   Three patients   (A) and (B) are stethoscopic and (C) a logarithmic phonocardiogram
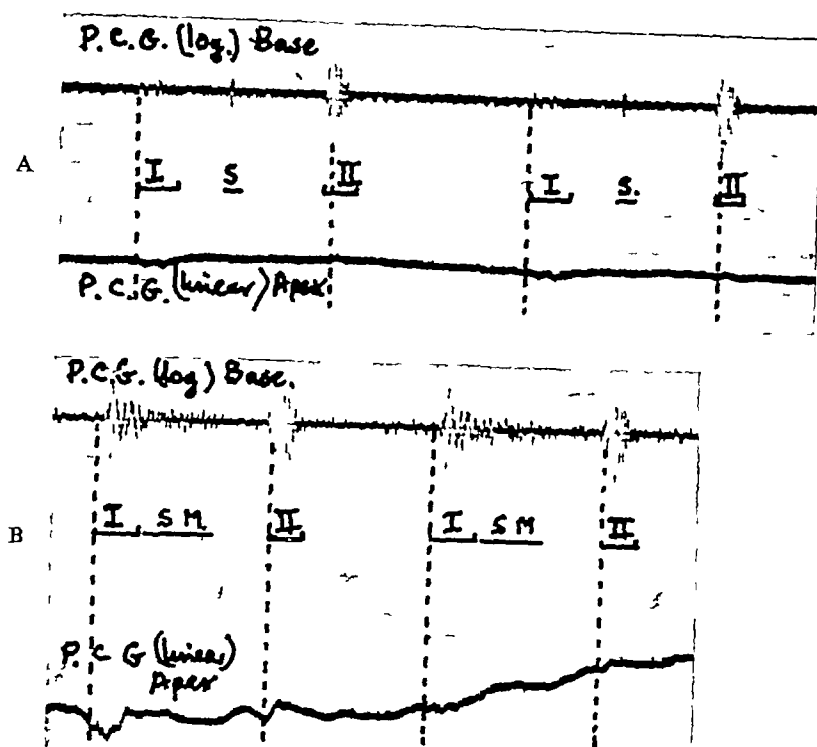
FIG 11   Hypertension—basal recordings   Two patients   Ringing aortic second sounds but no diastolic murmurs are present   A systolic gallop sound (S) is present in (A)

the T wave bears a sufficiently variable relationship to the second sound to make it valueless as an indication of the onset of the second heart sound It is believed that Evans' records of hypertension can bear a different interpretation if this is taken into account

SUMMARY AND CONCLUSIONS

An investigation was planned to test some of the phonocardiographic findings on heart murmurs announced by Evans (1947)   In order to do this it became necessary to construct a new phonocardiograph whose characteristics are described in Part I

No clear-cut distinction between the systolic murmurs found in valvular and congenital heart disease (57 cases) and those found in patients with no evidence of heart disease (27 cases) could be established by timing the onset of these murmurs against the S line of lead II of the electrocardiogram

The systolic and presystolic murmurs in 30 cases of mitral stenosis were found to be clearly distinguishable from one another in timing and mean frequency, as they were on clinical auscultation

No additional ætiological information to that collected clinically was found by a phonocardio graphic examination of 21 cases of aortic incompetence

In 20 cases of hypertension with a consistent diastolic blood pressure of over 100 mm none was found with an aortic diastolic murmur

For phonocardiography to be a useful aid in clinical cardiology it is necessary to use an instrument whose characteristics are known and satisfy certain basic considerations   The electrocardiogram alone is an unsatisfactory reference tracing for studying heart murmurs by phonocardiography as there is no strict co-relation between the electrical and mechanical events of the cardiac cycle

Although the phonocardiographic investigations recorded in this article are of a negative nature it is felt that phonocardiography can help the clinician in the diagnosis of heart murmurs, and work on these lines is progressing

It has been a great pleasure to work in close co operation with the Research Department of the Cam-

bridge Instrument Company, England, to whom my grateful thanks are offered

I wish to record my thanks to Professor Sir Lionel Whitby, Regius Professor of Physic at Cambridge, for much help and advice, to Dr Leslie B Cole of Addenbrooke s Hospital, Cambridge, for permission to use his cases and for his enthusiasm and advice, and to Dr William Evans for his generous advice and help

This work was undertaken during the tenure of an Elmore research studentship at the University of Cambridge

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THE NATURAL HISTORY OF CORONARY DISEASE
A CLINICAL AND EPIDEMIOLOGICAL STUDY

BY

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Since William Heberden wrote his classic account of angina pectoris in 1768 and Edward Jenner, in a letter to him ten years later, suggested the association of the syndrome with disease of the coronary arteries, the subject has continued to claim the interest and attention of physicians in each succeeding generation Taking this country alone and excluding living authorities, we have only to recall such names as Latham, Clifford Allbut, Osler, Mackenzie, and Lewis Symptomatology, both in their periods and since, has been the chief object of speculation and of study and although, with the aid of a more refined and intimate case-work, the subjective phenomena could even now be accorded a more detailed and accurate portraiture, the general clinical picture has been widely approved The physiological researches of Lewis and his colleagues have advanced our understanding of the pain which is the central symptom Morbid anatomy (especially in its bearing upon coronary occlusion as the cause of the status anginosus and succeeding cardiac failure), cardiography and radiography, have all made their contributions Prognosis, with the assistance of technical aids and in experienced hands, has achieved, perhaps, a slightly better precision Therapeutics, except insofar as a number of useless remedies have been discarded, have not registered any outstanding gains since Lauder Brunton's advocacy of the nitrites The course of the disease *in individuals* and the effects of symptomatic treatment have, in brief, been fairly adequately covered

The study of the disease *in the community*, on the other hand—its epidemiology and ætiology—have scarcely as yet received adequate consideration Where individual studies leave gaps in our knowledge social and statistical enquiry may have a contribution to make

When Heberden, who had no hospital associations, gave his paper to the Royal College of Physicians his experience of angina pectoris amounted to some 20 cases When he included the description in his "Commentaries" in 1782, his experience had extended to 100 cases Osler was admitted to the Fellowship of the Royal College of Physicians before he had seen a case in hospital or private practice Mackenzie, with all his earlier experience in general practice and later as a leading consultant in cardiology, wrote (as late as 1923) that 380 patients had consulted him for angina pectoris Today, as Cassidy (1946) remarks, "the modern cardiologist s name is legion" and "he counts his cases by thousands rather than hundreds" On both sides of the Atlantic the steadily rising incidence of coronary disease in recent decades has been noted, and it has been suspected that this trend, as indicated by mortality figures, is not wholly to be explained by such factors as the changing age-constitution of populations and by improved diagnosis and certification at death

In connection with ætiology, speculations have been frequently advanced concerning the influence of the manifold stresses inherent in the conditions of life and work that our industrial civilization has imposed, and concerning the possible effects of nicotine That hereditary predisposition plays some part has long been allowed The assumption that angina pectoris and coronary occlusion are, in the main, expressive of nothing more than the arterial degenerations that accompany the inescapable process of ageing has not seemed satisfactory in the absence of a definition of ageing and in the case of a disease so common at the summit of a man s energies and achievement, and now so frequently recorded in the fifth and sixth decades (i e at ages 40–59), not infrequently in the fourth decade (30–39), and sometimes even earlier (20–29) Adherents of the so-called psychosomatic school of medicine—perhaps beause their approach has been too predominantly psycho-analytical and because they have tended to see selected examples rather

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than the general run of cases that pass through the hands of the family practitioner, the physician and the cardiologist—have almost certainly overstressed the influence of specific emotional conflict Those cardiologists, on the other hand, who have doubted the ætiological contributions of mental stress and fatigue, with or without the addition of the more ordinary types of day-to-day anxiety, may be shown to have erred in another direction and to have attached altogether too little importance to the body-mind relationship and to the exacting circumstances of modern modes of life and work, which are in many respects as different as it is possible to imagine from those enjoyed or endured by our more slowly moving agricultural forebears

THE SCOPE OF THE ENQUIRY

The present study falls into two parts The first is based upon a statistical analysis of material to be found in the Reports of the Registrar-General (covering a recent twenty-five year period) in its bearing upon the deaths from coronary disease in England and Wales This study has involved correlations with age, sex, social class, and occupation and geographical distributions, and has taken into particular account the secular trend of the disease during the period under review The second is based upon an analysis of the clinical histories of a series of cases seen by one of us (J A R) during a closely similar period of 23 years in the course of consulting practice

In this manner, and by pooling our experience, it seemed to us that we could, in some measure, combine the advantages of two of the more important methods of socio-medical enquiry *Statistical surveys* with correlations based upon official mortality returns rely for their validities upon the large numbers employed While recognizing that the original data upon which the figures are based have been subscribed by a host of observers of varying reliability, we may yet accept that there is a sufficient smoothing out of error, by virtue of quantity, to compensate for qualitative inaccuracy As regards the diagnosis of most cases of fatal angina pectoris and coronary occlusion in the period covered by the statistical survey, there should not have been great difficulties, so familiar had the symptom-picture of the first stage of the disease and, commonly, of the second stage, by then become Nevertheless, steps were taken, as will be seen, to meet the criticism that the diagnosis of coronary thrombosis or occlusion has been made with increasing frequency throughout the period under review, and that certain vague nomenclatures, such as ' myocardial degeneration '' (which have long been loosely used in death certi-

ficates) must now be giving place to more accurate classifications and thereby accounting in large part for the increased rates of mortality

A *clinical survey*, even when conducted in retrospect—given that sufficient attention has been paid to possible personal, familial and habitual influences and to social and occupational factors and to the age at onset of the disease—has some, but only some, of the merits of a planned socio-medical enquiry As a study in morbidity (and this is especially so in the case of diseases that run a long course) it may be considered as a useful supplement to mortality studies, for these can give no indication of age at the onset of the symptoms or of the conditions of life and work then obtaining, and they cannot, as a rule, attempt correlations with other ætiological factors than sex, social class, occupation, and geography Nor can they throw light upon the various durations of the disease As a rule, however, the numbers available for a personal clinical study of this kind are very small by comparison with those required by the statistical epidemiologist and often some necessary evidence is found to have been omitted or recorded in a form unsuitable for abstraction Conclusions drawn from the physician's numerical analyses must consequently be cautious The majority of cases in the clinical series were seen on one occasion only, some on two, three or more occasions, a few were seen so often and over such long periods of time as to allow of a growing intimacy both with the manifestations and varied course of the malady and with the affairs and personalities of its victims An obvious disadvantage of the series relates to the fact that the cases were, inevitably, socially selected An advantage, on the other hand, may be discerned in the fact that the information was collected by a single observer, and that his interest at the time was concentrated on the whole disease rather than upon any particular aspect of it

THE STATISTICAL STUDY

In 1926 the reported deaths from angina pectoris in England and Wales totalled 1,880 In 1945 the number of deaths ascribed to disease of the coronary arteries and angina pectoris was 25,012, of which 16,514 occurred among males and 8,498 among females During the intervening years the mortality from this cause of death has steadily increased and, in this connection, the comment by the Registrar-General (text for the years 1938–9) is of interest

' The progressive increase since 1920 in the standardized mortality assigned to coronary disease and angina pectoris continued without a break in 1938 and 1939 In 1920 the rates were

32 per million for males and 13 for females, and by 1939 they were twelve or thirteen times as great (406 and 153 respectively) To what extent this increase is explained by changing fashion in death certification, leading to transfer of deaths from myocardial and cardiovascular degeneration groups, and to what extent it is real, is difficult to ascertain "

The present study, based on the statistics relating to the period 1921–45, was undertaken with the aim of attempting to shed some light on the increased mortality from coronary disease and to observe its social and geographical distribution in England and Wales and its sex relationship

If the increment that has ostensibly occurred in the mortality has been obtained at the expense of the myocardial group, it is important that the composition of these groups should be uniform or stable during the period of observation In the present study the following sub-headings and their attached numerical identification in the list of the International Classification of Causes of Death were adopted as suitable criteria

	Period	Sub-headings
Myocardial group	1921–30	Fatty heart 90 (5)
	,,	Other or unspecified myocardial diseases 90 (7)
	,,	Arteriosclerosis without record of cerebral vascular lesion 91 (b) (2)
	1931–9	Myocardial degeneration 93 (b)
	,,	Myocarditis not distinguished as acute or chronic 93 (c)
	,,	Arteriosclerosis without record of cerebral vascular lesion 97 (3)
	1940–5	Myocardial degeneration, infarction, sclerosis and other chronic myocarditis 93 (c)
	,,	Myocarditis not distinguished as acute or chronic 93 (d)
Coronary disease	1921–30	Angina pectoris 89
	1931–9 and 1940–5	Diseases of the coronary arteries, angina pectoris 94

Secular Trend

In discussing the secular trend of the mortality from any disease or disease-groups over a long series of years, it is essential to be mindful of difficulties that do arise These may be listed as follows

(a) Changing fashion in diagnosis
(b) Changes in the International Classification of Causes of Death
(c) The abandonment by the Registrar-General of a priority classification and his acceptance of the

sequence as stated by the doctor when more than one cause of death is mentioned on the death certificate

While allowance has been made by the Registrar-General for the influence of (b) and (c) in statistics published for years since 1931, the impact of (a) remains an unknown quantity There also exists another influential factor in the trend of the all ages mortality, namely the effect of change in the age composition of the population The extent to which this has occurred, even during the relatively short period under review, is manifest in the following figures indicating the proportional age distribution of the population in 1921 and 1945

TABLE I

CHANGING AGE OF POPULATION

Year	Age groups				All ages
	0–14	15–44	45–64	65+	
1921 pop	29	47	18	6	100
1945 ,,	21	46	23	10	100

The proportion of the population in the age group 45–64 years increased by nearly 30 per cent, and at age 65+ by nearly 70 per cent, during this time interval of 25 years It is possible to make allowance for the influence of the ageing factor on the death-rate by calculating the comparative mortality index This index, which was devised by Dr Percy Stocks, " expresses each cause of mortality of each year as a ratio of that of 1938 adopted as the base after adjustment for age differences in the population exposed to risk "

Since the diseases that are being studied occur in adult life, and predominantly after the age of 30, the index, in the present instance, was calculated for age 35 years and upwards The results for the period 1921 to 1939 for males and females are shown in Fig 1 and 2, to which was added, as a matter of interest, the curve of the mortality from arteriosclerosis with a record of cerebral vascular lesion

The upward direction of each of the curves is quite a definite feature of the graphs, but, for both sexes, the gradient is steepest for coronary disease If three points of time be taken—1921, 1931, and 1939—the comparative mortality index for coronary disease for males was 0 10, 0 47 and 1 13, the corresponding values for females were 0 09, 0 42 and 1 08 The graphs also reveal

(1) The very close alignment between the trend of the mortality from the myocardial group and arteriosclerosis, particularly for females

COMPARATIVE MORTALITY INDEX AT AGE 35+ FOR MALES

FOR MYOCARDIAL DISEASE
CORONARY   " "
ARTERIO SCLEROSIS WITH RECORD OF
CEREBRAL VASCULAR LESION
IN ENGLAND AND WALES 1921-39

——— MYOCARDIAL DISEASE
- - - CORONARY   " "
× × × ARTERIO SCLEROSIS WITH RECORD OF
      CEREBRAL VASCULAR LESION
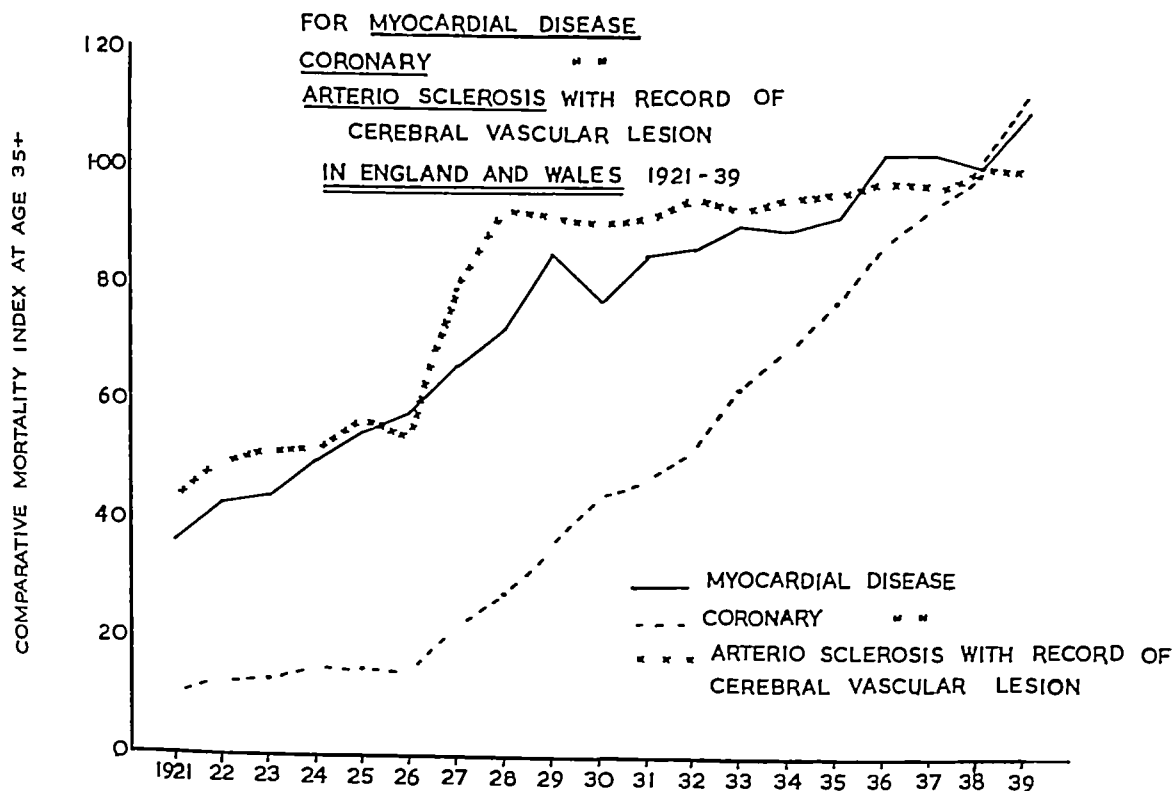
Fig 1 —Comparative mortality index at age 35+ for males for myocardial disease, coronary disease, and arterio-sclerosis with record of cerebral vascular lesion, in England and Wales 1921–39

(2) The increment in the death-rate from arterio-sclerosis with a record of cerebral vascular lesion between 1926 and 1928, an increase so great and so abrupt as to suggest that it indicates a change in " book-keeping " rather than anything specific in the disease itself

Since the progressive increase in each of the three causes of death is evident, it is pardonable to make a digression here to ascertain if such increment has been due to a transference of deaths from other forms of circulatory disease On this particular issue the following statistics, published by the Registrar-General in the text of the report for the years 1938–9, are instructive As regards the male mortality, which is the more important, the incre-ment in the death-rates at ages when circulatory disease is classified into two groups, A and B, was as shown in Table II

The figures suggest that some transference may have occurred from B to A, but certainly not sufficient to account for the vast increase observable in the latter To quote the Registrar-General " Such

TABLE II

INCREASE (+) OR DECREASE (−) IN RATES PER
MILLION FROM 1921–30 TO 1939

Age group	(A) Coronary Myocardial Arteriosclerosis Senility	(B) Valvular and " other heart " disease
	Males	Males
45—	+581	−284
50—	+1377	−369
55—	+2420	−737
60—	+4110	−1477
65—	+6114	−2806
70—	+9674	−3994
75+	+20856	−5861

transfer could, however, account for only a fraction of the increase registered amongst males for degenerative diseases affecting the myocardium and vascular system " The position would thus seem

COMPARATIVE MORTALITY INDEX AT AGE 35+ FOR FEMALES FOR
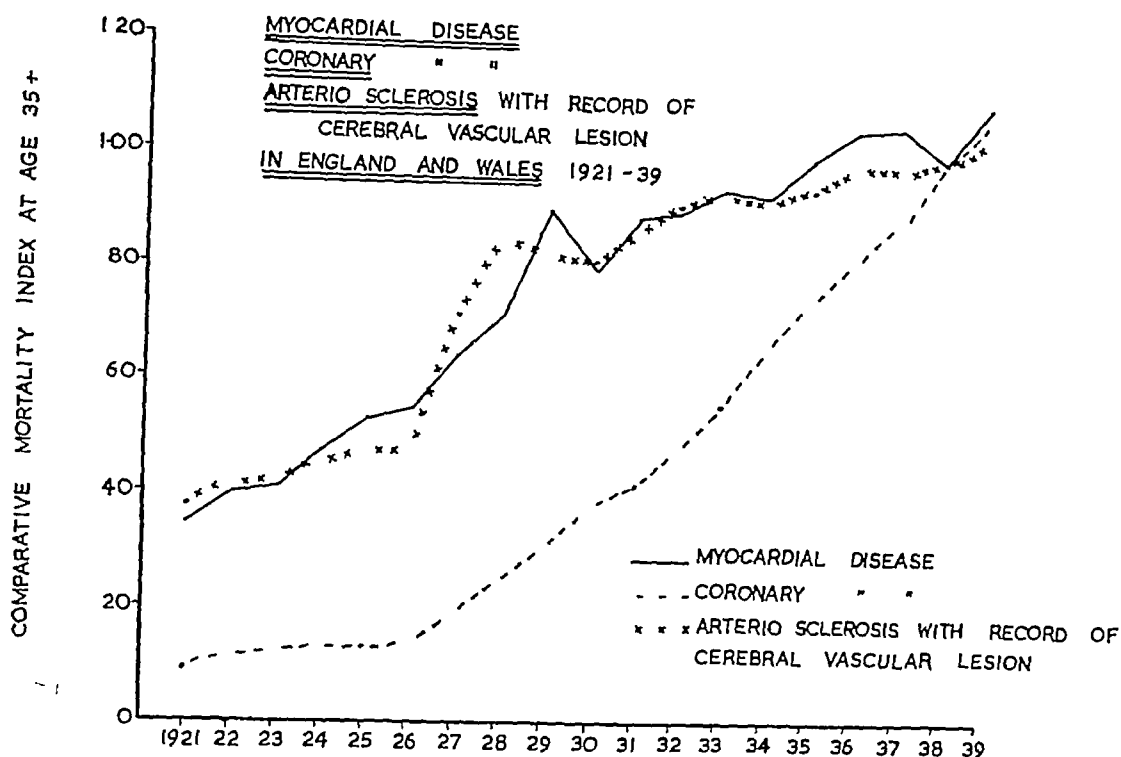
FIG 2—Comparative mortality index at age 35+ for females for myocardial disease coronary disease and arteriosclerosis with record of cerebral vascular lesion, in England and Wales 1921-39

to be that, up to 1939, coronary and myocardial disease were each increasing but not doing so mainly at the expense of the residual circulatory forms, and that the rate of increase was much greater in respect of the mortality from coronary disease But the similarity in the trend of the respective mortality of the two disease-groups ended in 1939 because the subsequent statistical experience, especially since 1941, has been entirely different The comparative mortality index for coronary disease in males in 1945, was 1 43, or 43 per cent greater than the death rate in 1938, whereas the myocardial index was 0 76, or 24 per cent in defect of the 1938 standard Similarly for females, the 1945 index for coronary mortality was 1 38, or 38 per cent greater than that in 1938, but the myocardial ratio was 0 80, or 20 per cent in defect It would thus seem that there has been either (a) a real decrease in myocardial mortality, or (b) a change in certification, observable since 1940, and that some deaths, previously attributed to myocardial causes, are now ascribed to one or other of the circulatory forms The divergence in point

of time is too abrupt and sudden to indicate (a), and (b) would therefore offer the more sensible explanation

Mortality According to Age

(1) *Coronary disease* While a picture of mortality based on a rate or ratio for combined ages even though such values be adjusted for effects of ageing of the population, is informative, it nevertheless lacks the clarification that a study of age specific rates of mortality can afford For this reason the average annual death-rates in age groups from coronary disease in the periods 1921-30, 1931-39 and 1940-45 (excluding 1944), and the percentage increments relative to the first epoch, are given in Table III The death rates at ages in the periods 1921-30 and 1931-39 were adjusted (by the application of conversion ratios) so as to make them comparable with those based on the revised classification that became operative in and after 1940 In the interpretation of the results it is essential to bear in mind that the time intervals are different,

THE DEATH RATES PER MILLION OF POPULATION IN AGE GROUPS FOR CORONARY DISEASE IN ENGLAND
AND WALES FOR CERTAIN PERIODS

Coronary Disease

Age group	Males						Females					
	Period			Percentage compared with 1921–30			Period			Percentage compared with 1921–30		
	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5
35—	16	46	69	100	288	431	4	12	16	100	300	400
40—	37	124	206	100	335	557	8	24	36	100	300	450
45—	75	282	466	100	376	621	16	53	86	100	331	538
50—	147	576	916	100	392	623	34	117	186	100	344	547
55—	266	963	1571	100	362	591	65	243	397	100	374	611
60—	439	1523	2380	100	347	542	136	510	771	100	375	567
65—	653	2247	3417	100	344	523	242	897	1446	100	371	598
70—	829	3067	4403	100	370	531	339	1338	2149	100	395	634
75+	913	3735	5582	100	409	611	437	1960	3019	100	449	691

being approximately ten years between the first and second epoch and approximately seven years between the second and third   Broadly speaking the statistical pattern for both sexes is similar   Between age 40 and 75 years there was an increment of approximately 250 per cent in the mortality in each of the intervening age groups in 1931–9 as compared with 1921–30   The increase continued and in 1941–5 ultimately amounted to approximately 450 per cent   The statistics also indicate that in middle age, 40–55 years, the male death-rate was increasing more rapidly than that for females, whereas in old age the position was reversed   Since, on the whole, there has been a fairly uniform increase in the mortality throughout life, the increment which has occurred in middle age being not very dissimilar from that for older people, it is extremely unlikely that transference of deaths from " old age " affords an adequate explanation of the increased mortality from coronary disease

(ii) *Myocardial disease*   The relevant statistics for myocardial disease are stated in Table IV   Here again there is a close agreement in the statistical experience of the two sexes   Between age 40 and 65 the rates increased approximately 50 per cent for both males and females in 1931–9 as compared with those in the initial period, subsequently, they decreased, with the result that in 1940–5 the ultimate excess, except at age 75+, was of the order of 30 per cent for males and 20 per cent for females

Transference of Myocardial Deaths

Attention has been previously drawn to the decline in the comparative mortality index, at age 35 years and upwards, for myocardial disease since

1941   It would appear from Table IV that each age was affected, as the death-rate in every age group in the period 1940–5 is lower than the corresponding value in 1931–9   This fact would seemingly indicate that some deaths previously certified as due to this cause are now ascribed to one or other of the forms of circulatory disease   The relevant questions then arise, is it possible

(1) To estimate the extent of this transposition?
(2) To ascertain if the coronary disease mortality has been credited with the transfer?

The clinical features of coronary thrombosis were first clearly presented in England by McNee (1925)   A lapse of fifteen years before the acceptance of a more precise classification of causes of cardiac deaths became general would not be remarkable   The following procedure was adopted to provide an answer for which no exact precision is claimed, but only a fair degree of approximation   It was assumed that the age-specific death-rates for both myocardial and coronary disease increased linearly during the period 1931–9, which means that the equation of a straight line describes their course during the years in question   The constants obtained from these linear equations for each age group were utilized to forecast the expected age-specific death-rates in 1945   Admittedly, extrapolates obtained from such limited experience, and for so relatively wide an interval of time, are not entirely satisfactory   Nevertheless, the procedure offers the only adequate method of approach   The comparison of the actual and predicted rates of mortality at ages (adjusted for change in classification) for each of the two causes of death is made

TABLE IV

THE DEATH-RATES PER MILLION OF POPULATION IN AGE GROUPS FOR MYOCARDIAL DISEASE IN ENGLAND AND WALES FOR CERTAIN EPOCHS

Myocardial Disease

Age group	Males						Females					
	Period			Percentage compared with 1921–30			Period			Percentage compared with 1921–30		
	1921–30	1931–9	1940–5	1921–30	1931–9	1940–45	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5
35—	55	97	70	100	176	127	48	101	65	100	210	135
40—	116	214	152	100	185	131	91	184	122	100	202	134
45—	322	462	343	100	143	107	242	365	269	100	151	111
50—	628	1003	796	100	160	127	473	706	539	100	149	114
55—	1254	1932	1725	100	154	137	917	1376	1091	100	150	119
60—	2617	3935	3471	100	150	133	1928	2928	2371	100	152	123
65—	5392	7725	7027	100	143	131	3880	6008	5067	100	155	131
70—	10,213	15,904	13,922	100	156	136	7672	12,520	11 144	100	163	145
75+	23,777	40,988	39,153	100	172	165	20,508	36,382	35,099	100	177	171

in Table V For coronary disease it will be seen that, for each age group, with one single exception (45–50 for males), the expected death-rate is greater than the actual death-rate For males, apart from age 70+, the excess at the other ages is of the order of 10 per cent For females the difference is somewhat greater Hence it would appear that the mortality from coronary disease is now increasing less rapidly than in the period before the war As was to be expected from the previous evidence, the gulf between the actual and predicted death rates in 1945 for myocardial disease is not only much wider but, as will be noted, the disparity is correlated with age for both sexes Up to age 55 the expected death-rate for males exceeds the actual by nearly 100 per cent The difference subsequently declines and after age 60 it amounts to approximately 50 per cent For females the difference is greatest at

TABLE V

THE ACTUAL AND EXPECTED DEATH-RATE PER MILLION OF POPULATION IN AGE GROUPS FROM CORONARY AND MYOCARDIAL DISEASE IN ENGLAND AND WALES IN 1945

	Coronary Disease			*Myocardial Disease*		
	Males			Males		
Age group	Actual death rate	Expected death rate	Difference as percentage of actual death rate	Actual death rate	Expected death rate	Difference as percentage of actual death rate
45—	542	542	0	280	547	−95
50—	1045	1168	−12	659	1353	−105
55—	1838	2008	−9	1424	2666	−87
60—	2924	3140	−7	3065	5483	−79
65—	4066	4313	−6	6377	9424	−48
70—	5256	6126	−17	12,812	19,430	−52
75+	6477	7723	−19	36,250	54,681	−51
	Females			Females		
45—	98	108	−10	197	421	−114
50—	234	237	−1	461	838	−82
55—	447	517	−16	947	1524	−61
60—	893	1039	−16	2097	3378	−61
65—	1680	1850	−10	4542	7024	−55
70—	2600	2787	−7	10 445	15,262	−46
75+	3392	4390	−29	33 517	47,289	−41

TABLE VI

THE ACTUAL AND POTENTIAL " DEATHS PER MILLION OF POPULATION IN AGE GROUPS IN 1945 FROM CORONARY DISEASE ASSUMING THE MORTALITY HAS BEEN INCREASED BY TRANSFER FROM THE MYOCARDIAL GROUP

Age group	Potential death rate = expected coronary death-rate plus difference between actual and expected myocardial death rate			
	Males		Females	
	Actual death rate	Potential death rate	Actual death rate	Potential death-rate
45—	542	542+ 267= 809	98	108— 224= 332
50—	1045	1168+ 694= 1862	234	237± 377= 614
55—	1838	2008+ 1242= 3250	447	517+ 577= 1094
60—	2924	3140+ 2418= 5558	893	1039± 1282= 2321
65—	4066	4313+ 3047= 7360	1680	1850± 2482= 4332
70—	5256	6126± 6618=12,744	2600	2787— 4817= 7604
75±	6477	7723±18,431=26,154	3392	4390±13,772=18,162

45–50 years—114 per cent—but no undue importance may be given to this value because the mortality at this particular age is low At the other ages the decline approximates to that for the male sex, with the result that in old age the expected death-rate is roughly 45 per cent in excess of the actual

Since the " calculated " age-specific death-rates from coronary disease in 1945 are greater than the actual, it would suggest either

(1) that there has been little or no transference from the myocardial group to this category, or

(2) that coronary disease in itself has decreased and that the high mortality now observable is actually due to a transfer of myocardial deaths

Hence it is of interest to assess what would have been the position if the transposition had occurred The most likely magnitude of the transfer would have been the excess of the expected over the actual death-rates from myocardial causes The addition of this difference to the expected coronary death-rate would yield what we have called the " potential death-rate " from coronary disease in 1945 The result shown in Table VI indicates that if such a change or transfer occurred the coronary death-rate up to age 75 years for males would be doubled and, beyond that age, would be four times its existing size The alteration in the female mortality would have been even greater

Sex Ratio

Although the increment in the mortality from coronary disease has not been dissimilar for the two sexes, the dominance of the male mortality over that for females is excessive, as will be seen in Table VII which shows the male–female sex ratio at the various age groups and, in addition, similar

TABLE VII

SHOWING THE SEX RATIO $\left(\frac{M}{F}\right)$ AT AGE GROUPS FOR CORONARY AND MYOCARDIAL MORTALITY IN ENGLAND AND WALES AT DIFFERENT PERIODS

	Coronary Disease			Myocardial Disease		
Age group	1921–30	1931–9	1940–3	1921–30	1931–9	1940–3
35	4 0	3 8	4 3	1 15	0 96	1·08
40	4 6	5 2	5 7	1 27	1 16	1 25
45	4 7	5 3	5 4	1 33	1 27	1 28
50	4 3	4 9	4 9	1 33	1 42	1 48
55	4 1	4 0	4 0	1 37	1 40	1 58
60	3 2	3 0	3 1	1 36	1 34	1 46
65	2 7	2 5	2 4	1 39	1 29	1 39
70	2 4	2 3	2·0	1 33	1 27	1 25
75+	2 1	1 9	1 8	1 16	1 13	1 12

SMR

ANGINA
PECTORIS

220
200
180
160
140
120
100
80
60
40
20

BLACK = MALES

WHITE = WIVES

CLASS | I | II | III | IV | V
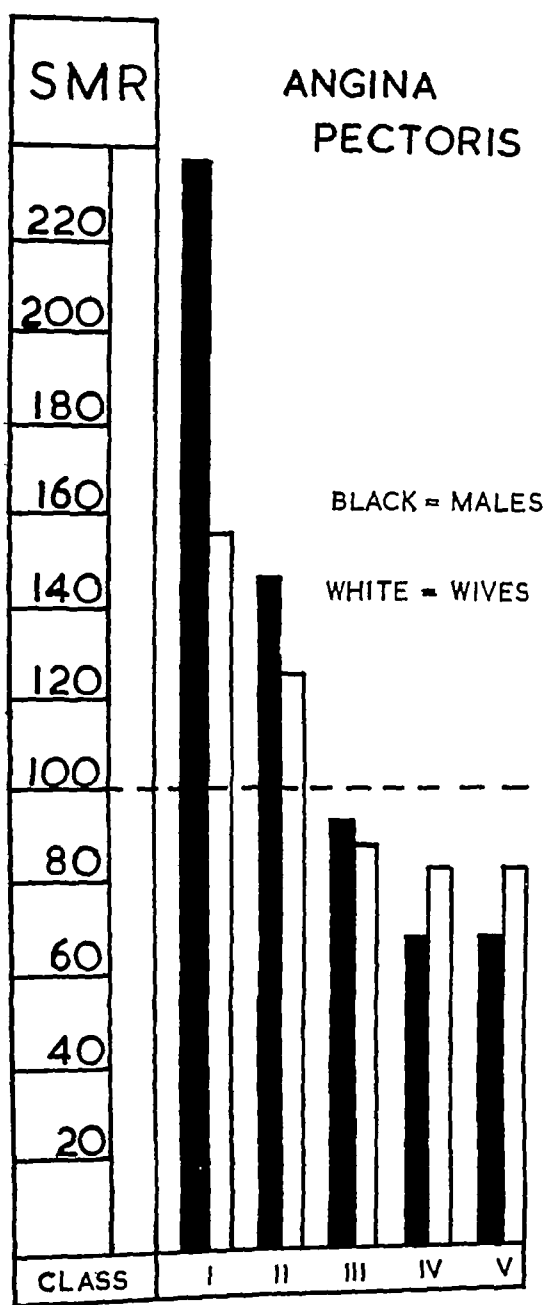
FIG 3 —Standard mortality ratio from angina pectoris for men divided according to their social class as in the Registrar General s reports, and for wives

values for the myocardial diseases For the latter the male excess, after age 45, is of the order of 30 per cent, with no definite age association indicated in any of the three time periods On the other hand, for coronary disease there is a decided relationship with age, observable in each of the three epochs For example in 1940–5 the male death rate at age 40–50 was more than 5 times greater than for females, at 55–60 the ratio drops to 4 0 and at 75+ it is less than 2

This negative correlation of the sex ratio for coronary disease with age and the relative absence of any association in the case of myocardial disease suggests the impact of some factor detrimental to males in the causation of coronary disease The most obvious sex discriminant is an occupational influence and, in this respect, the statistics available in the Registrar-General's Occupational Supplement for 1930–2 are instructive In this very interesting and valuable report, the Registrar General published the mortality from various diseases according to five social classes The constitution of these social classes has so often been described that it is unnecessary at this stage to enlarge on their structure It is sufficient to state that Class I is largely composed of professional workers, Class III represents skilled artisans and Class V unskilled workers—the two residual groups being intermediate to the contiguous grades The correlation between the mortality from angina pectoris and social level is depicted in Fig 3 in which it will be seen that, for both men and wives the decrease in mortality with descent in the social grading is clearly indicated For males in Class I the mortality is 137 per cent in excess of the average for all males aged 20–65 years It is 4 per cent in defect for skilled workers, and for unskilled workers the mortality is 33 per cent below the expected or normal value If the occupations comprising the various social orders are studied separately the comparison is even more strikingly depicted, as will be seen from the mortality ratios in four occupations showing the highest and lowest values respectively (Table VIII)

These results clearly indicate the influence of type of work on the liability to death from coronary disease, since the four occupations having the highest ratios are those requiring not only a high degree of mental activity but also involve considerable anxiety and stress in their performance For workers at the other end of the scale life is from the point of view of mental activity, relatively less exacting and it would appear that their risk of dying from coronary disease is much more remote

Realizing then that social or occupational status is a correlate of the mortality from coronary disease, it was of interest to ascertain if men and wives within

TABLE VIII

MALE OCCUPATIONS OF HIGHEST AND LOWEST
MORTALITY FROM CORONARY DISEASE

Highest		Lowest	
	S M R		S M R
Physicians sur-geons	368	Coal miners be-low ground, en-gaged in other work	40
Proprietors of wholesale business	235	Stone miners and quarriers	38
Judges, barristers, solicitors	227	Agricultural and gardeners labourers	32
Clergymen of Anglican Church	218	Workers in chemi-cal processes	20

All males = 100

(The standardized mortality ratio (S M R) is the percentage ratio of the deaths actually registered in an occupation to those which would be expected to occur if the workers at age periods in that occupation experienced the age specific death rates for all males)

the same social pattern were equally at risk The sex ratios of their mortality in three age groups for angina pectoris and myocardial disease were evaluated and the results are stated in Table IX For myocardial disease the variation in the size of the ratio, either according to social gradient or age, is of a slight order, whereas for angina pectoris the position is different, age is a factor, but social class more so The importance of the latter is most obvious in the age period 45–55 in Social Class I, in which the male death-rate is almost ten times greater than that for wives, for skilled workers (Class III) the sex ratio is five, and it drops to 3 in the lowest social class Why, it may be asked, is the ratio dominantly male in Social Class I at age 45–55? The most likely answer would seem to be

that the workers included therein at this age period are those who have usually reached the peak of their professional careers and are exposed to the maximal strain associated with their particular responsibilities Mentally, their tempo of life is fast and, as the sex ratio indicates, they are not " masters of their fate "

Cassidy, in his Harveian Oration (*loc cit*), asks the following question " Is it possible that in the remarkable sex-incidence of coronary disease we may find some clue to aetiology? Can it be that masculinity predisposes one to coronary disease, and that feminity safeguards from it—that perhaps cholesteral metabolism is vitiated by maleness? " In this connection, it would seem important not to overlook the question of occupational influence and the fact that the mortality ratio of male professional workers to male manual workers is far higher than that of men to women

Geographical Distribution

Finally, in this epidemiological survey it was of interest to depict the geographical distribution of the mortality from coronary disease throughout the country A direct approach here is not possible because, although the Registrar-General has pub-lished, since 1940, the number of deaths from coronary disease in the several areas of the country, the age and sex composition of the population exposed to risk in these areas is unknown In the present instance, an attempt was made to override this difficulty by comparing, for the twelve major geographical regions, the actual and the expected number of coronary deaths—the latter being esti-mated from proportional mortality ratios The procedure of estimation was as follows The pro-portion which the coronary deaths in age groups in England and Wales bear to the deaths from all causes at the corresponding ages was estimated for

TABLE IX

SHOWING THE SEX RATIO$\left(\frac{M}{F}\right)$OF THE MORTALITY FROM ANGINA PECTORIS AND MYOCARDIAL DISEASE
ACCORDING TO SOCIAL CLASS IN ENGLAND AND WALES IN 1930-2

	Angina Pectoris				Myocardial Disease		
Age group	Social Class				Social Class		
	I	III	V		I	III	V
45–55	9 9	5 3	3 3		2 2	1 3	1 4
55–65	4 6	3 4	2 4		1 9	1 3	1 2
65–70	5 0	2 4	2 2		1 9	1 4	1 4

the triennium 1941–3 and the results are shown in Table X

TABLE X

RATIO OF CORONARY DEATHS PER 1000 TO THOSE FROM ALL CAUSES AT SPECIFIC AGE PERIODS

Age group Years	Male	Female
—40	2 6	1 0
40—	35 0	9 1
45—	55·0	14 4
50—	71 5	21 8
55—	79 1	33 4
60—	78 4	41 2
65—	74 2	48 0
70—	70 0	41 3
75—	47 6	33 1
80+	29 0	20 6

These percentage ratios were accepted as " standard ratios " and applied to the All Causes deaths at the corresponding ages in each areal unit On this basis the expected number of coronary deaths in each of the twelve major geographical regions of the country was obtained and then compared with the actual number of recorded coronary deaths in the three-year period 1941–3 Proportional mortality, which is the relationship of two variables, when used irrespective of age and time for comparative purpose, has recognized limitations Possible allowance has been made for these factors in the present instance, but it is nevertheless advisable to test the validity of the adopted procedure

There being no published statistics in areal units for coronary deaths prior to 1940 a test was made using nephritis as a criterion The expected deaths from this disease for the two years 1931–2 were estimated in two ways

(a) By the method of proportional mortality as previously described for coronary disease, allowance being made for the urban and rural character of the region

(b) By indirect standardization, i e applying death-rates at ages from nephritis in the County Boroughs, Urban and Rural Districts in England and Wales to the populations exposed to risk in the specific areal or regional unit

The expected number of deaths obtained on each of the two hypotheses were then related to those actually recorded The test was made on the data for Warwickshire which contains the most populous County Borough—Birmingham—in England and Wales The results are shown in Table XI As will be noted the ratios obtained by the two different methods, are in very close accord Hence it would seem that by using proportional mortality

TABLE XI

RATIO OF ACTUAL TO EXPECTED DEATHS FROM NEPHRITIS ESTIMATED IN TWO WAYS

Birmingham		Warwickshire			
C B		Urban		Rural	
M	F	M	F	M	F
(a) 82	67	90	110	69	94
(b) 81	65	97	112	64	84

in the manner indicated, it is possible to estimate, with some degree of accuracy, the number of deaths from coronary disease that might be legitimately expected to occur in each of the twelve major divisions of the country

The ratios of the actual and expected number of coronary deaths for males and females during the triennium 1941–3 have been worked out for these areas, both for males and females, there is a definite zoning of the mortality Greater London has an excess of 21 per cent above the average or expected number for males, next in sequence is the group of residual South-Eastern Counties with an excess of 11 per cent, followed by North I where the actual deaths exceed the expected by 3 per cent There is a large belt composed of North IV, Mid lands I and II and Wales I in which the mortality is approximately 15 per cent below the average The divergence between the results in Wales is noteworthy In Wales I (South Wales) the recorded deaths are 15 per cent in defect of the expected number, whereas in Wales II (North Wales) the difference is one of 3 per cent

The ratios for females are closely correlated with those for males, areas with high or low male mortality being also those in which the female deaths are also either in excess or defect of the expected value The reason for these apparent geographical disparities in the size of the ratios is not readily apparent Do they represent a true accounting or are they the resultant effect of differences in the social structure of the populations living in the different area units? It is not possible to give a definite answer owing to lack of appropriate data and it is obvious from previous evidence, that social stratification is an influential factor in determining the mortality from coronary disease

THE CLINICAL STUDY

General observations The period covered in this part of the enquiry is approximately 23 years (1920–42), but the majority of the cases were seen

during a 15-year period (between 1925–39) The experience was that of a general medical consulting practice The patients included in the series would thus represent, in the main, Social Classes I and II of the Registrar-General's classification by occupations, with a few from Social Class III After excluding dubious cases the notes of 243 cases remained, these were primarily classified as *angina pectoris* (144 cases) or as *coronary thrombosis* (99 cases) Only 2 cases were accepted in which a history of characteristic pain was lacking No cases of angina vasomotoria or of so-called " hypertensive failure " (Clifford Allbutt's " cardiac defeat ") were included, although high blood pressures must have added a load to hearts embarrassed by coronary disease in a number of cases No cases were included of aortic valvular disease or aneurysm or of pernicious anæmia This total of 243 cases of coronary disease represents approximately 1 7 per cent of all new private cases seen in consultation during this period As no special reasons obtained for regarding the writer (J A R) as a cardiologist, cases of heart disease should not have been referred for an opinion in any undue proportion It is not known how the proportion would compare with that discoverable in family practices of varying type or locality

Of the 243 cases in the series 164 were males and 79 females, giving an approximate ratio of M2 F1 This corresponds closely with the sex ratio revealed by the All Ages Deaths from coronary disease in 1945 Cassidy (*loc cit*), in a more predominantly cardiological practice and in a much larger series of cases of coronary disease, records a ratio of M3 5 F1 Of the 164 male cases, 97 (60%) were primarily classified as angina pectoris and 67 (40%) as coronary thrombosis Of the 79 female cases, 47 (60%) were primarily classified as angina pectoris and 32 (40%) as coronary thrombosis The relative incidence of effort angina and of coronary thrombosis was thus similar in the two sexes On re perusing the case-histories, however, it was found that angina pectoris (effort angina) had been preceded by an earlier account of a severe prolonged attack of pain, often lasting two hours or more (but without the more catastrophic picture of a severe coronary lesion) in an appreciable proportion of the cases While most cases of effort angina probably start as such and may be assumed to be due to coronary sclerosis without occlusion, or even to coronary spasm (in association, commonly, with one or more of the general manifestations of hyperpiesia), it would seem probable that small coronary occlusions (sclerotic or thrombotic), often unrecognized at the time, may not infrequently initiate the liability to effort angina

In the 144 cases (both sexes), primarily classified as angina pectoris, there was a previous history of a prolonged attack of pain—not necessarily associated with effort—in 15 (10%) In 99 cases (both sexes), primarily classified as coronary thrombosis, there was a preceding history of effort angina in 28 (28%) Subsequent histories of the surviving cases of coronary thrombosis were not available in a sufficient number to allow of an estimate of the frequency with which this accident is followed by effort angina It is well recognized that in some cases recovery is so far complete as to be followed by neither pain nor dyspnœa on exertion, sometimes for long periods The above observations do little more than lend support to the common clinical and pathological opinion that effort angina and the status anginosus of coronary occlusion are expressions only of different stages or accidents in the same disease They also suggest that the course and behaviour of the disease in the two sexes is similar, although its frequency is greater in men It is clear that the two clinical syndromes, expressing coronary sclerosis and sclerotic or thrombotic occlusion respectively, can legitimately be discussed together in any consideration of epidemiology or of possible ætiological factors

Age of Onset

Epidemiological studies of chronic types of disease based upon mortality figures are, as has been indicated, in a measure unsatisfactory in that they can give no account of the age of onset or of the occupation or other circumstances obtaining at the time of inception of the disease The occupation recorded in a certificate is the last one preceding death In 149 male cases and 69 female cases in this series it was possible to deduce, from the age of the patient noted at the time of the first examination and from the historical notes, the age *at onset* with a margin of error probably not exceeding one year.

TABLE XII

AGE OF ONSET OF CORONARY DISEASE

Age at onset	Males (youngest)	34	Females (youngest)	35
	(oldest)	90	(oldest)	83

	Age distribution at onset (males) in 149 cases	Age distribution at onset (females) in 69 cases
Under 36	2	1
36–40	2	0
41–45	12	1
46–50	23	7
51–55	21	5
56–60	23	12
61–65	28	19
Over 65	38	24

In 26 per cent of the male cases and 13 per cent of the female cases the age of onset was 50 years or less, in 74 per cent of the male and 87 per cent of the female cases the age of onset was over 50 years The numbers are small but they suggest that the factors accounting for male preponderance are more operative in the earlier or middle than in the later period of adult life This assumption is supported by the evidence that in England and Wales in 1946 the deaths from coronary disease amongst males aged 30–50 years constituted 6 per cent of the deaths from all causes in this age group, whereas the proportion for females was only 1 4 per cent At age 50 years and upwards the corresponding values for males and females were 9 and 5 per cent respectively Newman (1946) has reported on 50 young cases of coronary occlusion from the British armed forces which came under observation during the second world war Of these, 39 were fatal (33 dying suddenly), and the diagnosis was established at necropsy Coronary occlusion without thrombosis was recorded in 29 of the cases, and with thrombosis in 10 The youngest case was aged twenty and no less than 22 were within the age group 20–29 Of the 50 cases, 45 had been graded ' fit ' or ' I ' on joining the Service There was only one female case in the series, but the ratio of men to women in the Services was in the neighbourhood of 10 or 15 1 A further reference to this group will be made in the section dealing with aetiology

Occupation

In 100 male cases and 47 female cases at ages 65 or less the *profession or trade*, if any, was sufficiently clearly indicated to allow of an occupational classification Of the women 11 were single and of these 5 were gainfully occupied The married women were classified as " housewives , *four of them were, in addition, gainfully occupied*

TABLE XIII
Occupations (males, aged 65 or less)
(100 cases)

Business (including merchants managers, stock exchange, shopkeepers etc)	39
Physicians and surgeons	19
Clergy	6
Officers (R N , Army, R A F)	6
Justices judges, solicitors	6
Engineers	4

The remainder, each item of which scored less than a 4 per cent incidence, belonged to a great variety of professions and trades and included, for example, a peer of the realm, the driver of a hearse, a colonial rancher, a chief railway clerk, a pro-fessor of archæology, and the manager of a skating rink Of males aged 50 or less at onset (total 39 cases), 12 (30%) were business men, and 11 (28%) physicians or surgeons It has been previously indicated that according to the standardized mortality ratios published by the Registrar General for the period 1930–2 the highest value was that for the medical profession (see Table VIII)

TABLE XIV
Occupations (females, aged 65 or less)
(47 cases)

Married women (classified as housewives)	32
Married women (engaged additionally in gainful occupations)	4
Single women (unoccupied or not stated)	6
Single women (gainfully occupied)	5

Special Stresses

In rather more than a third of all the cases (both sexes) there was a clear enough history of occupational, domestic or other stress preceding the onset of symptoms to warrant a consideration of these factors (in concert with the sex and occupational histories) as having a possible bearing upon ætiology There was a record of " special stress " preceding the onset of symptoms (in most cases over a prolonged period) in 62 male cases and 27 female cases Of those cases in which there was no record of special stress a considerable proportion were in retirement on account of age The absence from the case notes of a history of special stress in these and the remaining cases did not necessarily exclude its occurrence and in some cases the occupation alone made its operations probable The occurrence of stress is thus under—rather than over—estimated In a few cases sudden death or a coronary occlusion was shortly preceded by some grave strain or anxiety Under the heading of special stress were included entries relating to mental overwork or worry in business or the home or in both, heavy public or other responsibilities, or other forms of sustained anxiety In a few cases intimate knowledge of the patient's affairs was accepted as evidence of stress in the absence of a specific entry relating to it As the neurotic temperament " (in distinction from an ambitious or conscientious personality pattern) has sometimes been held to be an ætiological factor, entries bearing on this, or its combination with special stress, were also abstracted (Table XV)

Thus specific records of special stress occurred in at least 38 per cent of males and 34 per cent of females in the whole series Of 9 (married and single) gainfully occupied women, all may be said to have been working under stress The 5 occupied single women included a nurse, still working to within 6 months of onset at the age of 62, the *headmistress*

TABLE XV

MALES (164 cases)

A "Special stress"	B Neurotic temperament plus ' special stress '	C Neurotic temperament without record of special stress "	No specific record
60 (37%)	2 (1%)	5 (3%)	97 (60%)

FEMALES (79 cases)

22 (28%)	5 (6%)	1 (1%)	51 (65%)

of a big girls' school with many additional public duties and a history of severe mental shock preceding onset at the age of 51, a business woman, excessively nervous and conscientious, with onset at 62, a religious sister in charge of a large students' hostel, with a strong family history of coronary disease and onset at 50, and a massage and physiotherapy instructor, greatly overworked and with a high sense of duty, with onset at 46 If the male cases aged 50 and under at the time of onset are taken, there is a specific history of " special stress " in 21 (54%) out of 39 cases, 6 out of 9 female cases (married and single) aged 50 or under at onset (66%) gave a history of special stress The occupations of the single women have been noted above Of the duties of the modern housewife it may at least be said that her domestic responsibilities are seldom light, that her children, her husband and her home tend to be more seriously considered by her as the generations pass, that she often undertakes additional civic or social responsibilities and, in the social classes studied, commonly has a share in her husband's problems which was denied to the Victorian woman After age 65 a high proportion of patients were in retirement, some of them were in their seventh or eighth decade, ' special stress ' would naturally, therefore, have become a less frequent entry Reliable histories of stress in earlier life are not easily obtained from the elderly, but it was noted as having been operative at some stage in 10 cases (25%) out of 41 males, and in 5 cases (18%) out of 27 females in the later age groups (i e 65 or over)

It would be unwise to infer too much from the above figures It is evident that stresses, both intellectual and emotional, must generally tend to accumulate towards the zenith of a career and to be fewer at its beginning or towards its close It must also be allowed that, in the taking of clinical histories modifiable conditions of life may be more carefully sought for in the case of younger and still occupied subjects But neither of these considerations compels the exclusion of continuing or recurrent stress as an ætiological factor The sex

and occupational associations reviewed in the statistical study have already drawn attention to its probable importance

Physical stress In a few cases golf or tennis was continued into middle or later life, as an addition to an exacting professional career, a few patients had been athletes in their youth, one patient was a blacksmith There was, however, no strong evidence to suggest that physical over-activity was a factor of comparable importance with mental or emotional over-activity This is again in accordance with the conclusions to be drawn from the occupational incidence of coronary disease provided by the mortality data, which reveal the relatively low incidence of angina pectoris in manual workers as compared with the professions, to which attention has already been drawn

Associated Illnesses

The association of angina pectoris and coronary thrombosis with gall-stones or cholecystitis has often been remarked The incidence of clinically recognized gall-bladder disease in the general population within the age-period under consideration is not known, but it is doubtful whether it would be found to be as high as 9 per cent in males On the general experience of hospital and private

TABLE XVI

ASSOCIATED ILLNESSES

	Males (164)	*Females* (79)
Gallstones and cholecystitis	15 (9%)	6 (7%)
Duodenal ulcer	10 (6%)	Nil
(One case had a history of both duodenal ulcer and gall-stones, one of a duodenal and a gastric ulcer)		
Other vascular lesions	7 (4%)	6 (7%)
Obesity	5 (3%)	7 (9%)
Migraine	5 (3%)	Nil
Diabetes or glycosuria	4 (2%)	4 (5%)

practice, peptic ulceration has a much higher frequency than gall-bladder disease The incidence of duodenal and gastric ulcer in male factory populations and some other employments, according to Doll and Avery Jones (personal communication), is between 5 and 6 per cent A figure of 6 per cent of cases of peptic ulcer in the males of this series is not necessarily, therefore, in excess of anticipation Migraine has been stated to be common in the histories of anginal cases The incidence recorded in this series is probably underestimated (a) because a history of it was not particularly sought for, and (b) because it would not as a rule, be spontaneously mentioned by patients in a request for an account of

" previous illnesses " If there is more than a chance association between migraine and angina, it is probably related to the fact that the same temperament predisposes both to migraine and angina, that both are noted as *commoner in professional workers*, and both tend to run in families The incidence of *obesity* has also been underestimated in this series, as only the more obvious cases received specific entry Although weights were routinely recorded, except in bedridden cases, heights were not, so that height-weight ratios could not be determined It is doubtful whether obesity is causally related to coronary disease, although it is well known that it may add an extra load to an already incommoded heart

Other vascular disease Cassidy (*loc cit*) found that hyperpiesis (e g a blood pressure of 160 systolic and 100 diastolic or more) was present in nearly 70 per cent of his cases lacking a coincident or recent history of coronary occlusion In the 150 cases of this series, in which the notes included a clear record, blood pressures of 160/100 or over were recorded at some stage of the disease in 66 cases (44%), a further 7 cases (5%) gave systolic readings of 170 or over with diastolic figures below 100 Very high readings were frequently recorded in uncomplicated angina pectoris and low readings were by no means the rule after a coronary occlusion If we accept angina pectoris and coronary occlusion as local manifestations of a more general arterial disease, it might be expected that vascular changes or accidents affecting other parts of the body (e g cerebral hæmorrhage or thrombosis, retinal hæmorrhage or peripheral arterio-sclerosis with intermittent claudication) would be a common association In fact there was, up to the date of the last entry, a history of other local vascular symptoms preceding or succeeding the onset of coronary disease in only 7 male cases (4%) and 6 female cases (7%) The reasons for local selective actions in arteriosclerosis have yet to be explained Normal blood pressures do not exclude its presence

Taking the men and women together there was a record of syphilis in 3 cases, but none showed signs of cardio-aortic syphilis, of coincidental hyperthyroidism in one case, of hypochromic anæmia in 2 cases (one with a *coronary* thrombosis and the other with effort angina and a history of angina pectoris in four *generations*), of asthma in 2 cases, of gout in 2 cases, of paralysis agitans in one case, of diverticulitis in one case There was one case with an earlier history of unilateral pyonephrosis and one of chronic Bright's disease Four patients had a synchronous carcinoma of the stomach or bowel, one had had a malignant ovarian cyst removed

Tobacco and Alcohol

Detailed records of the amount smoked were not kept Although a large number of men were considerable smokers, in only 2 cases was there a note of " *excessive* " tobacco consumption, in 4 there was a record of alcoholism, and in 1 of an excessive *use of both tobacco and alcohol* Although the majority of men with angina pectoris were smokers, non-smokers are certainly not immune Among the women of the period and the age groups reviewed smoking was rare

Family History

Family histories, at no time easy to secure in accurate form, are inevitably defective for this further reason—that sympathetic *consideration often* compels the avoidance of detailed enquiries about cardiac illness and deaths in the parents or other near relatives of persons themselves the subjects of heart disease The physician is also faced with the difficulty of deciding in the case of coronary disease, whether to include only cardiac cases or all instances of arteriosclerotic illness in the families studied

Cassidy (*loc cit*) states that " family history played a part " in " almost exactly half his cases," but he supplies *no details* For the reasons given, family histories were not consistently enquired into in this series, in the anxious situations accompanying a coronary occlusion they were often not asked for There were, however, *positive family histories* of certain or probable coronary disease relating to a parent, a brother or *sister*, or others in the direct line in 12 male cases (7%) and in 8 female cases (10%) Among the males there was one instance of the same disease in a father and an uncle, one in a father and a brother, one in two brothers The probable influence of heredity (whether operating through physical, mental, or temperamental predisposing factors or some combination of these) is supported by such histories as the following, which are taken from the present series

(a) One medical man, who developed his symptoms before the age of 39, lost a brother from coronary thrombosis in his early thirties

(b) One religious sister, who developed angina pectoris at 50, gave a history of cardiac deaths in her father, paternal grandfather and grandmother and a paternal great grandmother and of others in these generations, usually between the ages of 50 and 60 Her mother's side of the family was healthy

(c) An unoccupied spinster, developing symptoms at 60, gave a history of angina or cardiac deaths in her father, and her second and third brothers, and

of " strokes " in her fourth brother and her second, sixth and eighth sisters

(d) Twin brothers (probably monozygotic twins), both formerly Army officers of high distinction and mental attainments, and having a remarkable identity of thought and taste, developed coronary disease within a few years of each other

Of 20 cases (male and female) with positive family histories of angina, coronary thrombosis, or middle-age cardiac deaths, 13 (65%) developed symptoms at the age of 50 or less   In some other chronic diseases such as gout, due in part to an inherited factor, symptoms are apt to develop earlier in life where the family history is strong   Whatever the actual contribution of heredity to ætiology may be, the rising mortality from the disease and its occupational associations suggest that extraneous factors must be considered as of major importance

Prognosis

A study of the natural history of a disease would be incomplete without a consideration of prognosis   A knowledge of social or group experience has interest in itself and value alike for life assurance and individual assessments   Unfortunately, reliable statistical studies of prognosis are at all times difficult and this is especially so in the more chronic types of illness   There are many circumstances that militate against careful follow-up enquiry in cardiac disease, whether in hospital or consulting practice   While it has always been recognized that angina pectoris is a condition in which precise forecasts, whether in respect of survival or of degrees and durations of improvement are scarcely possible, so many are the variable factors concerned, it would yet be of value if we could discover the mean expectation of life in relation to age of onset, mode of onset, and perhaps to some other factors such as ranges of blood-pressure or the presence or absence of other evidences of arterial disease   It is well known that one man may die in his first attack and that another may live for 20 years or more   John Hunter, notwithstanding that he continued to suffer frequent pain, lived and worked for 20 years after his coronary occlusion at the age of 41   Cassidy (*loc cit*) records two cases of patients surviving for more than 30 years, and one of a woman who died suddenly at 82, having experienced effort angina from the age of 30

Where coronary thrombosis, as distinct from effort angina, is concerned there was a tendency to take too grave a view of prognosis following the recognition of the syndrome characteristic of the graver episodes which first became familiar in this country after the publication of McNee's paper (1925)   While a coronary occlusion accompanied

2D

or shortly followed by congestive failure or arrhythmia is commonly succeeded by death in hours, days, weeks, months or at the most a few years, a study of bad attacks in respect of the severity and duration of the pain, but lacking these complications, may reveal a longer expectation of life, sometimes with a resumption of normal activities for considerable periods   With still slighter attacks the outlook may prove to be even better   From the present series three illustrative cases may be selected, each one clinically characteristic and confirmed by cardiographic and subsequent history

(a) A surgeon, working under a very great physical, mental and emotional stress and a heavy smoker, developed effort angina at the age of 39   Some months later, at the age of 40, he had an extremely severe coronary thrombosis from which, for a time, it seemed almost impossible that he would recover   There were secondary complications in the form of an extensive pulmonary infarction with a pleural effusion and a prolonged phase of mental confusion   Within two years he was able to return to his hospital duties and thereafter continued them for a further 13 years, to the time of his death although always handicapped by an effort angina and latterly also by intermittent claudication

(b) A general practitioner, after prolonged hard work and a sad bereavement, had an attack of coronary thrombosis at the age of 45   Three years previously he had had a cholecystectomy for gall-stones   He had otherwise been very healthy and a fine athlete in his youth   He retired from practice early, but was able to do a good deal of steady work in his garden and even for a time to play 36 holes of golf in a day   He remained liable to pain down both arms on walking after meals   He lived happily for 15 years and died during an afternoon nap in his garden

(c) A masseuse and physiotherapist, the head of a large hospital department and a woman of great energy and with a high sense of duty, had a moderately severe coronary thrombosis at the age of 46   Subsequently she had symptoms of cholecystitis and at one time some gouty symptoms   She was still working in a private capacity 20 years after the original episode

These three patients were all under 50 at the time of their first symptoms, all overworked, two were endowed with restless energy   About such younger cases, it may be reasonably argued that they lack the more widespread degenerative changes in the vascular system which develop in the later decades and that the coronary occlusion in their case, is more in the nature of a local accident   As coronary occlusion commonly affects subsequent efficiency and the expectation of life in an adverse way, the interval that elapses between the first onset of effort

angina and a first coronary thrombosis or a pro-
longed attack of pain suggesting a small occlusion,
might seem to have some bearing upon the prog-
nosis of the uncomplicated condition   This interval
could be estimated in 49 cases only   The approxi-
mate duration of uncomplicated angina of effort
was estimated in 87 cases

TABLE XVII

Interval between first onset of angina and first symptoms of coronary occlusion	Duration of history in surviving cases of angina uncomplicated by coronary occlusion (when last examined)
Men and women (49 cases)	Men and women (82 cases)
	cases		cases

Less than   5 years   43   Less than   5 years   69
More than 5   ,   4   More than 5   ,   4
More than 10   ,,   2   More than 10   ,,   8
                                   Twenty years   1

A physician is likely to see an undue proportion of
cases in the earlier stages of the disease when they
can be referred to him in his consulting room   As,
furthermore, the numbers are small and a follow-up
enquiry over a further 10 years or more might have
been necessary in order to secure the final informa-
tion in some cases, no conclusion can be drawn from
this series with regard to the mean expectation of
life at ages in cases of uncomplicated effort angina
or of coronary thrombosis   Such conclusions
could only be derived from collaborative morbidity
studies undertaken by a number of general practi-
tioners covering sufficiently representative social
groups and areas of the country and over a sufficient
period of time

Case fatality   According to the data compiled
by the Nuffield Bureau of Health and Sickness
Records, Oxford, there were 196 patients with coro-
nary disease admitted to the twenty-five hospitals
within the Oxfordshire region during the three years
1945-47   The case fatality has been grouped
according to age and sex and the All Ages fatality
for men and women did not differ appreciably, being
61 and 66 per cent respectively   But at ages under
65 years the rate for males was much higher than
that for females   Hence this small sample of
hospital statistics, assuming it to be a microcosm
of general outside experience, indicates that not only
is the disease relatively more concentrated in middle-
age in males than in females, but also that it is more
fatal to them   It should be noted, however, that
cases admitted to hospital are likely to include a
high proportion of serious cases   There are, in

fact, no means at present of ascertaining the case
fatality at ages in the general community

The above observations can only be held to indi
cate some broad probabilities in the disease as a
whole in the groups studied

ÆTIOLOGY REVIEWED

Where the predisposing and precipitating factors
in a disease are several and there is no known
specific agent of extraneous origin—a situation that
obtains in many of the chronic endemic diseases of
today (such as hyperpiesia and coronary disease,
peptic ulcer, the chronic rheumatic diseases and the
psychoneuroses)—and where, furthermore, the
suspected factors must operate in varying combina-
tion and degree in different individuals, it is impos-
sible, in the present state of our knowledge, to
assess the full significance and relative importance
of any one factor   In favour, however, of each of
the five factors—familial predisposition, sex, ageing
certain types of professional employment, and mental
and emotional stress—there is, as has been shown
in the two main sections of this paper, considerable
presumptive evidence   Furthermore, these factors
often operate in conjunction

(a) maleness on account of the occupations which
it entails,

(b) the exacting character of sustained mental
work accompanying intellectual occupations and
posts involving heavy responsibilities,

(c) ageing, through mounting cares and the longer
exposure to stress,

(d) the emotional tensions that frequently, on the
one hand, accompany business, professional and
intellectual life and interruptions to it, and, on the
other, are expressions of

(e) the inheritance of an ambitious or con-
scientious personality pattern

We have, at present, no reliable evidence bearing
upon the association of special physical types   To
the physician in his consulting room patients with
angina pectoris present no such conformity of
pattern as can be observed, for instance, in a high
proportion of cases of duodenal ulcer   As in the
case of hyperpietics, many anginal subjects are of
good physique and have enjoyed excellent health in
earlier life,   this may have contributed to their
energetic habits

It may be argued, on the summary of the evidence
presented, that the older the patient developing
coronary disease the more have the ordinary
exigencies of the years subscribed to the general and
the coronary arterial degeneration, and that the
younger the patient the more are we entitled to
blame exceptional stress and the general pace and

fret of life in our modern mechanized world, in some cases with the added influence of familial predisposition Statistical studies and clinical observations would seem, in the main, to support one another Heberden's " disturbance of mind " is not to be ignored as a possible ætiological factor in coronary disease The very fact that any of the more urgent emotions can precipitate anginal pain, and occasionally even a coronary occlusion, should suggest the possibility that repeated emotional disturbance or prolonged anxiety may have a continuing adverse influence on the coronary vessels But, whatever part the stronger or more suppressed emotions may play, it would also seem, from the evidence here assembled, that sustained mental over-activity is another form of ' disturbance of mind " which must be taken into account and considered as capable of affecting the coronary circulation and eventually of causing damage to the arteries and the heart It is not possible to separate the effects of mental overwork and of the emotions (in the form of ordinary worries) which accompany it, but ' the neurotic temperament " had a low incidence in the clinical series Of all the extraneous factors *inimical to hyperpietic* subjects, with or without coronary disease, clinical experience, again and again, suggests that mental fatigue and strain and broken sleep are the most outstanding

The possibility remains that business and the professions tend continually to select from the population those types of person who are most predisposed to the disease This, however, would scarcely account for the steep rise in incidence and mortality within so short a period as a quarter of a century, and could only partially explain the occupational associations that have been demonstrated Although it cannot be excluded it does not seem necessary to assume a contribution to male proclivity on the part of the sex hormones, nor is there any suggestion of sex-linked inheritance

Of the *associated diseases* recorded in this series none would seem to be causally related, with the possible exception of gall-bladder disease There would be no sufficient reason to think of a relationship in this instance on the score of its observed frequency, but for the further clinical observation than an acute cholecystitis sometimes closely precedes or succeeds a coronary thrombosis This association should be worthy of more intimate study

Tobacco The fact that the majority of the women were non smokers and that the disease can occur in male non smokers, renders the influence of nicotine a doubtful one, although it cannot, as yet, be entirely excluded

The Youthful Cases

Separate consideration must be given to cases in the youngest age-group (20–35) Through the kindness of the author of the paper relating to service cases, based on Ministry of Pensions records (Newman, *loc cit*), we have been provided with notes, not included in his account, bearing upon arm of the service, rank, duties and pre-service occupation for the whole group and abstracts of findings at necropsy in 28 cases With the exception of one medical officer and two men promoted from the ranks during the war all were in the other ranks " category There was no indication in the brief records available that " special stress ' had been a likely or, at any rate, a sustained experience during service or in civil life Relatively few (15 out of 50) appear to have been on active combatant service Most of the cases would have fallen into the Registrar-General s Social Classes IV or V The ages of the 28 cases examined at necropsy varied from 20–35 In the majority of these arterial changes were so advanced as to suggest that the disease was of some standing and that it had probably started in civil life The pathological descriptions were not characteristic of syphilitic arteritis In 6 cases in the whole group the earlier civil occupation might have involved a lead hazard Reading these records and finding few indications of special occupational stress or other extraneous factor, one might at first feel inclined to reconsider some of the conclusions drawn in the preceding sections It must, however, be appreciated that these cases—even with the addition of others that may have escaped reporting—must represent a very insignificant proportion of the vast call-up for the three services during the war years Coronary disease at or below 35 is, in fact, a very rare event In 1946 the deaths from this cause in England and Wales under age 35 were 69 (0 37%) among 18,800 male deaths and 12 (0 12%) among 9,780 female deaths from coronary disease Where extraneous factors in early life are far to seek it may possibly be shown that genetic influences play a more important part than habits of life and work

HISTORICAL RETROSPECT

If the evidence here put forward in the form of joint clinical and epidemiological studies can be accepted as supporting the probable importance of an occupational type of hazard falling more heavily and more considerably with the passage of time upon those sections of the community whose work entails over-exertion of the mind rather than of the body it would seem proper to enquire into the changing social circumstances and habits of our

present era and to compare present with past historical experience It can scarcely be disputed (1) that the proportion of persons in the country who are professionally and intellectually employed has steadily risen since the industrial revolution of the nineteenth century in concert with such factors as increasing mechanization, the urbanization of the population (some 80 per cent of the people of England and Wales now live in urban areas as compared with 50 per cent a hundred years ago), and the extension of educational opportunity to all classes, (2) that the amount of mental work which can be accomplished by an individual in a day has considerably increased in the past century and especially in the last 25 years The train, the motor car, the aeroplane, the telegraphic, and telephonic and ordinary and air-mail postal services, the competent secretary, the typewriter and the dictaphone—all these may have made the conduct of affairs more possible, but they have also multiplied the number of intellectual operations—all occasioning vascular responses—that can be performed within a given space of time Competition in many spheres is more intense Interruptions to concentrated mental work, which tend to give rise to irritation or frustration, also having their well known vascular accompaniments, are probably far more numerous than formerly Refreshing sleep is more hardly won Emotions are more consistently repressed than is the case among more primitive or rural peoples Professional men a hundred years ago were often just as industrious, but the pace and tempo of their work and the knowledge and responsibilities required of them were of a different order In no calling, perhaps, would the contrasts be found to be greater than in the medical profession which, of all occupations, shows the highest mortality from coronary disease

SUMMARY

In the review of the mortality from coronary disease during the past 25 years in England and Wales the following points of interest emerge

The mortality amongst males and females aged 35 years and upwards in 1945 was 15 times greater than that in 1921 and the annual number of deaths from coronary disease is now approximately 25,000 *

The increments in the age specific death ratio rates for males and females were on the whole very similar, but there is evidence that in the age period 40–55 years the male death-rate was increasing more rapidly than that for females

Although there was a fair degree of parallelism in the secular trend of the mortality from coronary

and myocardial disease between 1921 and 1938, their subsequent statistical history differed, as the former has continued to increase whereas the latter declined In 1945 the comparative mortality index for myocardial disease was 24 per cent in defect of the 1938 standard for males and 20 per cent for females

The increase in the coronary disease mortality in the post-war period is unlikely to be wholly due to a transference of myocardial deaths because there is evidence that the coronary death-rate itself was increasing less rapidly in this period than in pre-war years—the actual death-rates at ages in 1945 being smaller than those predicted on the basis of the statistical experience relating to the period 1931–9

There is evidence of a distinct sex ratio The male death-rate in middle age is 5 times greater than that for females subsequently the ratio decreases with increasing age and at age 75+ it is less than 2 There is no similar magnitude in sex differentiation for myocardial disease nor is there any definite correlation with age

The most realistic explanation of this sex difference would be to ascribe it to an occupational or socio-economic influence The mortality from coronary disease amongst men aged 45–55 in Social Class I is nearly 10 times greater than that of wives, and men of this social category are mainly those in professions and business administration, in which the mental stress and strain accruing from their responsibilities is heavy

The mortality from coronary disease varies in different regions of the country The significance and meaning of this geographical variation cannot be accurately assessed owing to absence of requisite information on the age and social stratification of the population within each areal unit This knowledge is necessary because age and social status are important correlates of the mortality from the disease

The mortality from cerebral vascular disease showed an increase parallel with that for coronary disease up to 1939

The findings of the clinical study, making due allowance for its limitations, reveal a general conformity with those of the statistical study, and help to illustrate in a more detailed way some of the conclusions pertaining to possible causal influences Age of onset has been discussed It was 50 years or less in one-quarter of the men and one-eighth of the women The need and some directives for further enquiry into prognosis have been indicated

Disease of the coronary arteries has, finally, been considered briefly in its historical context and in particular relation to the remarkable social changes

* Deaths from angina pectoris and coronary disease in 1947 totalled 33,168

that have occurred since it was first described 180 years ago

CONCLUSIONS

The natural history of coronary disease has been discussed on the basis of a statistical study and of clinical experience, and in particular reference to its rising incidence and its social and occupational associations The effect of multiple cumulative causes has never, perhaps, been sufficiently emphasized in considering the genesis whether of symptoms or of pathological changes Effort angina induced by walking a given distance often occurs more readily (a) after a meal, (b) on a cold day, (c) in a state of anxiety or fatigue, than in the absence of one or more of these circumstances Similarly, the buttressing effects of the several factors reviewed in this paper may be regarded as subscribing to the slow genesis of the underlying arterial change There is nothing pointing to such alternative causal influences as infection or faulty nutrition The chemical pressor substances that determine the vascular reactions are endogenous and the product of nervous stimulation

Physicians are properly interested in the possible practical applications of their enquiries It seems at present remotely unlikely that we shall discover a "cure" for general arteriosclerosis or coronary artery disease—some part of the processes involved being irreversible In any case, diseases that attain a wide prevalence, having once been relatively rare, should be constantly considered with a view to a better understanding of how their incidence may be reduced—at least in those age-groups that cover the period of active work and citizenship

No such dramatic answers are here likely to be forthcoming as in the case of a bacterial or nutritional disease, but, even though they be counsels of perfection, we can at least argue that existing conditions of work in many professional and business careers impose strains which, when endured too long, are beyond physiological tolerance and that the conditions thus call for amendment, that members of predisposed families might sometimes be encouraged at an earlier stage, and even in the face of an activating conscience or ambition, to regulate their lives more rationally, that, in the field of personal hygiene, the organization of holidays, leisure, exercise and pleasurable relaxation is as sensible as attention to sanitary habits and balanced dietaries, and that the detection of hyperpiesia in the earlier phase by periodic health examinations could have value The fact remains, however, that mental activity, unlike manual labour, cannot be readily limited by legislation or arrested by the clock For some time to come we are, therefore, likely to witness a high toll of incapacitation and a sustained, perhaps increasing, death-rate from coronary artery disease affecting—and often at the time of their greatest efficiency—some of the more industrious members of the community in both sexes and in all classes, but more especially the male mental workers of the higher socio-economic grades This trend is likely to continue—the general ageing of the population making its contribution—until such time as our social reorganization is directed in new ways and in better measure to the promotion of healthy living through a more precise physiological and psychological understanding of man and his capacities and a deeper appreciation of his individual and social needs

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CONGENITAL AORTIC SEPTAL DEFECT

BY

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A defect in the wall of the ascending aorta leading to free communication with the adjacent pulmonary artery is a rare congenital abnormality   The opening in the anterior wall of the aorta is just above the semilunar cusps and leads directly into the pulmonary artery   Maude Abbott (1927) regarded it as a partial defect of the aortic septum, probably at the point where the distal bulbar swellings meet the aortic septum and above the junction of the aortic and interventricular septa   A commoner form of communication is between an aortic sinus and either the conus of the right ventricle (Abbott, 1919, Brown, 1939) or the right auricle (Goehring, 1920, Macleod, 1944), usually due to a ruptured congenital aneurysm of a sinus of Valsalva   Abbott (1937) also described a third rarer variety where a small hole in the aortic wall, just above the valves leads into the conus by an oblique channel   Here the aortic valves are usually bicuspid   An example of this type of abnormality was described by Rickards (1881)

This report concerns an example of the first of these anomalies, an example of value chiefly because there were no other congenital defects   The various features, clinical and pathological, to which the aortic septal patency had led, formed a combined picture of the pure defect that is rarely seen and therefore worth recording

CASE REPORT

A boy of 14 came under observation about two years before he died, when admitted to Horton Emergency Hospital in May 1943 for increasing dyspnœa on exertion and for palpitation   He had been breathless from infancy, and his activities had been severely curtailed since early childhood, though latterly he had done a light office job near his home   He had been prone to recurrent bronchitis and more recently to severe epistaxes

He was a pale stunted youth with a kyphotic chest   the anterior wall of which bulged forward

prominently on the left side   Cardiac pulsation was diffuse and thrusting, with the impulse maximal in the seventh space 16 cm   to the left of the midline   The beat was regular at a resting rate of 80 a minute   A diastolic thrill was easily palpable just inside the cardiac impulse and also to the left of the sternum at the base   A systolic and a diastolic murmur were heard all over the præcordia, the latter generally louder and more impressive and best heard in the pulmonary area and just internal to the impulse   The systolic element, loudest in the aortic area where it overshadowed the other, was well conducted to the root of the neck on each side   Both heart sounds were audible in all areas, and the pulmonary second sound was accentuated   The blood pressure was 130/40 and the pulse collapsing   Neither cyanosis nor clubbing were present, nor had he any congestive failure   Other systems were normal

Radioscopy showed a huge aneurysmal shadow comprising the pulmonary artery and aorta astride the greatly enlarged heart (Fig 1)   The aortic component was normally sited but very pulsatile, and no separate aortic knuckle could be seen   In oblique views the ascending aorta was prominent, and a barium swallow showed a combined aorto-pulmonary impression   Both ventricles were very large, the right larger than the left, and the right auricle was also thought to be moderately enlarged   The left auricle was flat in the right (I) oblique position (Fig 2), but the pulmonary artery radicles were all prominent and there was a marked hilar dance   Apart from their enlarged vessels the lung fields were normal   An electrocardiogram showed a rather low voltage R I, high R II and R III and a diphasic T I, but was otherwise unremarkable (Fig 3)

After keeping fairly fit and at work until October 1944 he then began to have recurrent faints and increasing breathlessness, for which he was re-admitted the following January   He was still pale, but now moderately cyanosed as well, though he
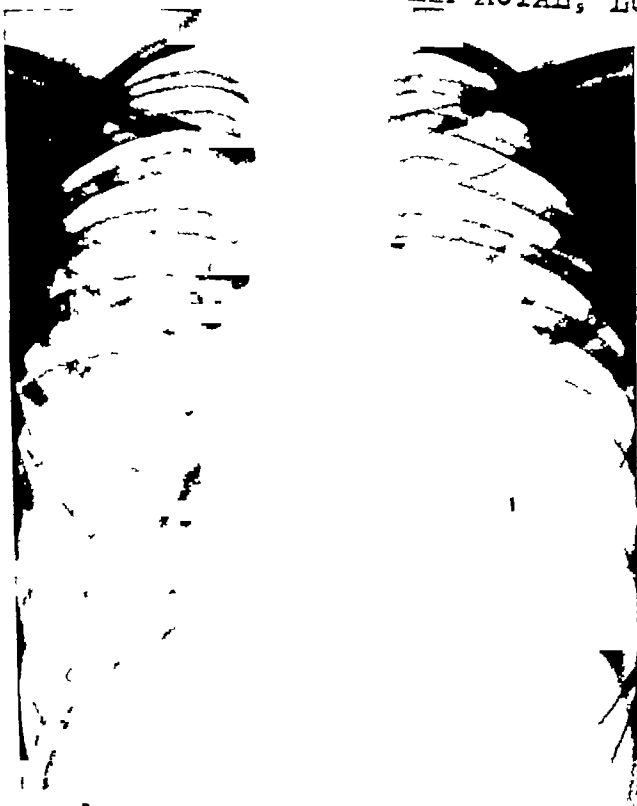
FIG 1 —Radiograph (anterior view) showing aorto-pulmonary sac, enlarged pulmonary vessels and enlarged ventricles   26/5/43

FIG 2 —Radiograph (right (I) oblique view) showing aorto-pulmonary sac and aortic arch above it, enlarged right ventricle and flat left auricle

had a normal blood count   There was no congestion and his cardiovascular signs were unaltered except that the heart s action was more forceful and further enlargement of the aneurysmal sac and of both ventricles was evident radiologically (Fig 4) He had repeated nose bleeds and also, from time to time severe sweating attacks which were quite unexplained   There was no evidence of endocarditis or other infective process   He improved gradually with rest and was convalescent by March

He was admitted for the last time seven months later in congestive heart failure   He had fallen ill a week before with catarrhal symptoms and was already in a grave state when admitted orthopnœic, moderately cyanosed and sweating profusely, though afebrile   The neck veins were much engorged the liver enlarged tender and pulsating, and there was dependent œdema   The left chest wall bulged even more than before and the action of the heart shook the whole thorax   The murmurs were unaltered except that the diastolic murmur was more obtrusive and now loudest in the mitral area   The
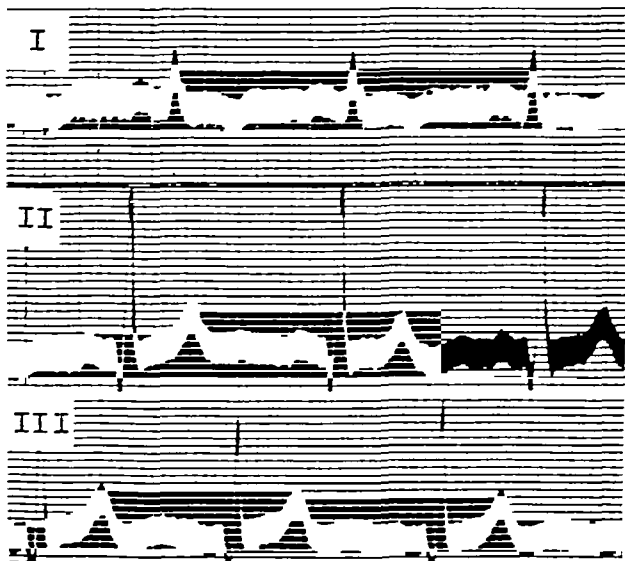
FIG 3 —Electrocardiogram

FIG 4 —Radiograph (anterior view) showing further enlargement of aorto-pulmonary sac and heart also more engorgement of lung vessels   22/4/44   The maximum transverse diameter is now 18 cm in a chest of 24 5 cm instead of 16/23 5 cm in 1943 (Fig 1)

pulmonary second sound was very loud   Rest, sedatives, and diuretics failed to give relief and he died suddenly a few days later

NECROPSY REPORT

The body was well nourished but undersized Both lungs were congested and there was excess of straw-coloured fluid in the pleural sacs and about 350 ml in the pericardium   The liver was enlarged and intensely congested

In situ the heart was surmounted by a large aneurysmal sac comprising the main pulmonary artery and the contiguous aorta (Fig 5)   The heart weighed 390 g and was greatly enlarged   Both ventricles were much hypertrophied and dilated, the right ventricle particularly   Their walls were of equal thickness, measuring 2 0 cm   across   In

FIG 5 —Necropsy specimen, anterior view showing the aneurysmal sac

contrast the auricles were not enlarged All the heart valves were normal, but the mitral ring took three fingers easily The interauricular and inter-ventricular septa were normal

The aneurysmal sac when opened showed a wide communication between the hugely dilated pulmonary artery and the base of the aorta just above the valves The defect measured 6 0 bv 5 0 cm Its edges were quite smooth and a small septal ridge formed its lower border between the aortic and pulmonary valves The valve cusps were all

normally sited The size of the defect was such that it gave an appearance of both ventricles opening through their respective valves into a common sac from which the right and left pulmonary arteries arose above and posteriorly and the aorta above, anteriorly and to the right The aorta itself was markedly hypoplastic measuring 4 1 cm in circumference at the top of the arch There was no coarctation the innominate, left common carotid and left subclavian arteries were normally sited and the fibrosed cord of the ductus was identified

above the aneurysmal sac   The main coronary vessels were normal in distribution and appearance

Other organs were normal apart from congestion   Sections of the lung tissue showed no endarteritis

CASES PREVIOUSLY REPORTED

Congenital aortic septal defects were reviewed by Hektoen in 1901, and by Abbott in 1927 and 1937   Hektoen had one case and collected nine others, one of these, mentioned already, was described by Rickards in 1881, and as it seems to belong to the rare third group of defect described by Abbott, we have not included it in this review   One further reported case was mentioned by Abbott in 1937, and Curtis Bain and Parkinson (1943) have since recorded another   The chief findings in these 11 cases are summarized in Table I

The average age at death was 14 years, but this approximate figure is much affected by two of the series who survived to 37 (Girard, 1895) and 48 (Moorhead and Smith, 1922) years respectively and in both of whom the septal defect was small   Three dying in early infancy (Gerhardt, 1874, Rauchfuss, 1878, Hektoen, 1901) are not fully described, and two (Baginsky, 1879, Cæsar, 1880) died respectively in childhood from convulsions during whooping cough and from brain abscess and tuberculous meningitis   Excluding all these, it is still evident, however, that the defect is a serious threat to life, for only one of the five remaining cases, including our own, survived beyond the second decade   Indeed, the most remarkable feature of our case was his survival until adolescence despite such a gross defect—a feature shared with the example reported by Bain and Parkinson (1943)

Though survival is variable, the physical limitations that the defect imposes appear to be almost uniform and always considerable   Symptoms of cardiac insufficiency from early infancy are always recorded where details are given, with one exception (Moorhead and Smith, 1922)   This exception was a man of 48, fit until 9 months before his death when symptoms began suddenly with severe chest pain and dyspnœa   Although the sudden onset, rapid course and previous good health suggested an acquired condition, the absence of disease in the aortic wall compelled the authors to regard the defect as congenital   With the two exceptions already noted (Baginsky, 1879, Cæsar, 1880) and another three for whom the cause of death was not stated, all the others died with congestive heart failure   There is no record of endocarditis as a complication, and the only mention of clubbing is by Cæsar (1880) and Bain and Parkinson (1943) who noted its moderate degree   In both these

clinical points there is a similarity to atrial septal defect (Bedford, Papp, and Parkinson, 1941)

The cardiac murmurs vary greatly   Cæsar (1880) specifically noted the absence of murmurs and both Wilks (1859) and Girard (1895) mentioned only a loud systolic murmur over the base of the heart   Fräntzel (1868), Baginsky (1879) and Moorhead and Smith (1922) all described a double murmur   A loud apical diastolic murmur alone with a thrill, was noted by Bain and Parkinson (1943)   It is evident that basically the signs are similar to those of any other free leakage from the aorta above the cusps as with a patent ductus, a ruptured aneurysm of a sinus of Valsalva, and an acquired communication between the aorta and pulmonary artery   Abbott (1937) suggested that diastolic accentuation might be due to secondary pulmonary insufficiency   Although a functional incompetency may well have been present in our case, none could be demonstrated at necropsy   Abbott also noted that the double murmur seemed to be more superficial than that of a patent ductus, an observation that we can confirm   As in our case, Moorhead and Smith (1922) found a large pulse pressure, the only other record (Bain and Parkinson 1943) failed to show it

The heart is always much enlarged   Dilatation and hypertrophy affect both ventricles, the right one especially   Aneurysmal dilatation of the pulmonary artery, by far the most impressive finding in our case, is by no means constant, a fact no doubt related to the frequency of small defects   Wilks (1859) drew attention, however, to the importance of pulmonary artery dilatation in his own case, and Bain and Parkinson (1943) found the pulmonary artery forming about two thirds of the aneurysmal sac

The site of the defect is remarkably constant and the lower border is formed by a smooth ridge of tissue separating the aortic and pulmonary sinuses   Though variable in size, the defect is generally small, about 1 cm in diameter   In our own case it was 6 cm × 5 cm, and, as in that of Bain and Parkinson (1943), was quite exceptional   The fine smooth edges are characteristic and distinguish the congenital from the commoner acquired communication between aorta and pulmonary artery (Brocq, 1885 and 1886)   Moreover, acquired defects are accompanied by aortic disease, commonly a ruptured aneurysm of the ascending aorta (Porter, 1942)

Judging from the few records, other congenital cardiovascular defects are usually absent   Fräntzel (1868) found the pulmonary artery distributed to the left lung only, the right pulmonary artery springing from the ascending aorta   Hektoen's case (1901),

TABLE I—DETAILS OF REPORTED CASES OF AORTIC SEPTAL DEFECT

Author	Age	Sex	History and symptoms	Signs	Mode of death	Description of defect, heart and vessels	Ductus	Other defects
Elliotson (1830)	Young	F	Cyanosed from birth Two weeks before death edema cyanosis orthopnea	Violent heart beat No clinical disease of heart	Congestive failure	Opening at point where aorta and pulmonary artery lie in contact, admitting at least a finger	Closed	None
Wilks (1859)	8 mth	F	From 4 months severe dyspnoea	Loud systolic over base and greater part of chest	Congestive failure	Midway between valves and innominate artery smooth edges, admitting goose quill Rt ventricle enlarged and pulmonary artery larger than aorta	Closed	Slight valvular patency of foramen ovale
Frantzel (1868)	25 yr	F	Dyspnoea and palpitation always	Diastolic maximal at base to right of sternum Systolic maximal at apex Changing murmurs in two months before death Harsh murmur over heart	Congestive failure	1 cm above aortic cusps circular 12 mm in diameter Left and right ventricles dilated and hypertrophied Aorta larger than pulmonary artery	Closed	Pulmonary artery distributed to Lt lung only Rt from ascending aorta
Gerhardt (1874)	5 mth	F	No details	No details	—	Just above valves size of half a lentil sharp margins	Not stated	None
Rauchfuss (1878)	Nursing	—	No details	No details	—	No details, but stated to be similar to Gerhardt's specimen	Closed	No details
Biginsky (1879)	4 yr	—	From 8 days repeated bronchitis and failure	Many systolic and diastolic murmurs Irregular rhythm	Convulsions pertussis	Triangular 0.5 cm above aortic cusps 1 cm in largest diameter Both ventricles hypertrophied Rt greater than Lt Wt 250 g	Closed	None
Cesar (1880)	9 yr	M	Cyanosed from 8 months Activity always limited	No murmurs Finger and toe clubbing from 3 months	Brain abscess and tub menin gitis	A little above aortic cusps size of sixpence Ascending aorta as big as in adult s	Not stated	Pulmonary valves perforated in several places
Girard (1895)	37 yr	M	From 1 year dyspnoea and cardiac distress	Systolic murmur with accentuated second sound Enlarged heart gallop rhythm	Congestive failure	1 cm above aortic cusps 1 cm in diameter Hypertrophy, especially of Rt ventricle Aorta larger than pulmonary artery Wt 670 g	Not stated	None
Hektoen (1901)	New born	M	No details	No details	—	2 cm above pulmonary cusps oval took tip of finger	Patent	Foramen ovale widely patent
Moorhead and Smith (1922)	48 yr	M	Sudden onset severe chest pain dyspnoea failing strength last 9 months	Double murmur resembling aortic leak to left of sternum Diastolic conducted to apex Large heart B P 160 40	Congestive failure	2 cm above pulmonary cusps took tip of finger opened into saccular dilatation of origin of aorta, which was stenosed above it	Closed	None
Bain and Parkinson (1913)	18 yr	M	Cyanosis and dyspnoea on exertion from infancy worse for 6 years Angina for 6 months	Cyanosis Moderate clubbing Large heart mainly to right with aneurysmal pulmonary artery Apical diastolic thrill and murmur B P 125/100	Congestive failure Sudden death	Single aorto pulmonary sac 8 × 7 × 6 cm Rt ventricle greatly enlarged Left ventricle normal	Not stated	Single brachio cephalic trunk Narrowed aortic orifice funnelled orifices of both pulmonary arteries Descending aorta arising from sac

dying at birth, had a patent ductus and widely patent foramen ovale, and Wilks' case (1859) at eight months also had a slight valvular patency of the foramen ovale Caesar (1880) found the pulmonary valves perforated in several places Bain and Parkinson (1943) found a common brachiocephalic trunk and funnelled openings from the sac into each main branch of the pulmonary artery Apart from these few, the aortic septal defect has been the sole congenital abnormality in all the recorded examples In contrast to this rarity of other defects, the communication produced by rupture of the right sinus of Valsalva into the conus is generally accompanied by a defect in the membranous part of the septum

DIAGNOSIS

The clinical recognition of congenital patency of the aortic septum is necessarily difficult, if only because of its rarity In none of the recorded cases was the diagnosis made in life, and it is doubtful how far it has, in fact, been considered hitherto Certainly in our own case it was not We believed we were dealing with a complicated defect, including a patent ductus arteriosus and probably an atrial septal defect, a combined condition that has been reported and has been diagnosed during life

The question remains whether a pure aortic septal defect can be recognized in life Acquired defects are not uncommonly recognized (Porter, 1942, Schattenberg and Harris, 1943) Primarily the diagnosis depends upon signs of a free leak from the aorta in the presence of a dilated pulmonary arterial tree and enlargement of both ventricles Such a combination is rare enough if we except patent ductus arteriosus either alone or along with an atrial septal defect When a patent ductus is the sole abnormality, enlargement of the heart and of the pulmonary artery and its branches is rarely so striking as that found with the large aortic septal defects in Bain and Parkinson's case and in our own As, however, the defect is often small, the same degree of enlargement is not always found

The difference from a patent ductus would then be much less obvious, and a distinction have to rest with the more superficial murmur When a patent ductus has anomalous signs, even no murmur, yet an unusually large pulmonary artery and branches, the difficulties in recognition may well be insuperable The injection of contrast media by the basilic vein is unlikely to provide conclusive evidence regarding the exact site of the aorto-pulmonary leak because dilution in the pulmonary artery by the aortic blood would make radiographic interpretation so difficult Perhaps in future retrograde angiocardiography may resolve the difficulty It is said to outline a patent ductus very clearly, and would almost certainly show the site and size of an aortic septal defect

Atrial septal defect alone, however, should be distinguishable, for here the auscultatory signs, though they may suggest an aortic leak, are not accompanied by excessive pulsation in the aorta and its main branches, nor by an increased pulse pressure Moreover, dyspnoea is late as a symptom, so late that a fair capacity for exertion is retained even with an enlarged heart well into middle life, a further contrast with aortic septal defect Also congestive failure is not found before the third decade of life, nor is the left ventricle characteristically involved in the cardiac enlargement Atrial septal defects also give characteristic findings on right heart catheterization (Howart, McMichael, and Sharpey Schafer, 1947)

If an atrial septal defect is accompanied by a patent ductus the similarity to a widely patent aortic septum is much more striking, especially in the degree of enlargement of right ventricle and pulmonary arteries But here again catheterization might be expected to reveal the atrial defect and suggest this combination from the associated physical signs

In so far as there is a common arterial sac with which both ventricles communicate, it might be expected that a persistent truncus arteriosus would most closely resemble a wide patency of the aortic septum, and yet, to judge from the records, this is not necessarily so There is general agreement on the poor prognosis of a truncus, the presence of a systolic murmur and thrill along with much enlargement of both ventricles, and a broad vascular pedicle But with a truncus, cyanosis is usually early and marked, although Taussig (1947) has recently claimed that this is the case only when the pulmonary circulation is maintained largely through the bronchial arteries The main pulmonary arteries are then either absent or rudimentary, and the radiological counterparts are the finding of small and ill-defined hilar shadows, a concave upper margin of the left border of the heart, and a hazy margin of the aortic arch due to the abnormally large superior bronchial arteries arising from it (Taussig, 1947) These points might clearly help to separate a truncus case of this type from a simple aortic septal defect, though in her recent book Taussig (1947) makes no reference to the latter

We also have to consider in differential diagnosis joint aortic and pulmonary valvular disease, aneurysm of a sinus of Valsalva, and an acquired as distinct from a congenital aortic septal defect None of these is likely to be traced to early child

hood by the symptoms and they all have the marks of acquired disease—rheumatic, syphilitic, or bacterial   An acquired aortic septal defect has a sudden, even dramatic, onset and runs a rapid course, commonly as a complication of an existing aortic aneurysm or, more rarely, of bacterial endarteritis   Evidence of an infection is in each condition more important as a guide than the details of cardiac enlargement or the nature of any murmurs   Combined enlargement of right and left ventricles, pulmonary arteries, and aortic root may be present in all of them as well as in congenital aortic septal defect, and along with this a double basal murmur, increased pulsation in the aorta and its branches, and an increased pulse pressure

Separation from congenital aortic septal defect may be feasible only if the probability of an acquired lesion in a subject past youth is integrated with collateral evidence of an infective cause

SUMMARY

An example of congenital aortic septal defect is described together with radiological and necropsy findings

Reported cases are reviewed and the diagnosis discussed

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THORACOSCOPY AS AN AID TO DIAGNOSIS IN CONGENITAL HEART DISEASE

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The advent of surgery in the treatment of congenital heart disease has meant that accuracy in the detailed diagnosis of the anatomy of the great vessels has become a matter of paramount importance instead of, as was formerly the case, an interesting mental exercise   Especially is this so when we are dealing with cyanotic heart disease, of which Fallot's tetralogy forms 70 per cent of cases   Anomalies additional to the classical four are not uncommon and may compel an exploratory thoracotomy before a decision can be made as to which side is the better surgical approach

Blalock (1946, 1947, and 1948) advocates that the approach be made on the side of the innominate artery, and points out that if the aortic arch is right-sided, the innominate artery is located on the left side   There is, however, as he states, a wide variation in the arteries arising from the aorta, and in some cases all four arteries have arisen independently from the aortic arch, there being no innominate artery at all   In 1947 he suggested the more extensive use of visualisation of the heart and great vessels by the injection of radio-opaque substances, but even this method leaves unsolved many questions that can only be answered after the vessels have been examined by direct vision

These difficulties were brought home to us in the recent case of a boy of 14 on whom we operated, with Fallot's tetralogy and a complete right-sided aorta   Following Blalock's suggestion that in such cases the innominate subclavian was more likely to be found in the left hemithorax, a left thoracotomy was performed   The aortic arch was found to be high in the mediastinum, with the subclavian coming directly from its upper medial aspect   There was a gap of about an inch between the aortic arch and the hypoplastic pulmonary artery, but it proved impossible to bridge this by the short avail-

able subclavian artery even though a maximal length had been freed and turned down

After this disappointment it was decided to attempt another diagnostic investigation in future cases, namely thoracoscopy after the induction of pneumothorax   Apart from the advantage that it is not such a major procedure as thoracotomy one hoped that this would supply the answer to many questions that exercise the mind of the surgeon before operating, such as the calibre and condition of the vessel wall, the extent of coarctation, and the condition of the aorta beyond the constriction   Thoracoscopy can be done on the table as a pre liminary to immediate operation, or it can be done some days previously

The following cases illustrate the use of this technique, the limitations and possibilities of which are still being investigated

Case 1   A puny but intelligent girl aged 7, was deeply cyanosed with gross parrot-beaked clubbing of fingers and toes   Clinically she appeared to be a case of dextrocardia with Fallot s tetralogy   On X-ray examination there was a pulsating shadow projecting from the heart on its left side and behind it   This shadow was provisionally interpreted as an enlarged auricle, possibly due to patent inter-auricular septum   Angiocardiography indicated that the ascending and transverse portions of the aortic arch and about one inch of the descending aorta were on the right side   Barium swallow showed no notching of the oesophagus to suggest a vessel crossing behind (Williams, 1947)

A left-sided pneumothorax was induced with 300 ml of air   The next day a thoracoscope (G U type 9 mm diameter) was inserted in the 6th left interspace near the angle of the rib, the patient lying on her right side   The lung was lying on the mediastinum but could be pushed out of the way

with the thoracoscope to reveal a " pulsating tumour " behind, the tumour was pink, smooth, retropleural and its pulsations were expansile, it emerged from the mediastinum and descended alongside the spine to disappear behind the lung It was in fact the aorta which had crossed over the spine from the right side The subclavian artery was concealed by the lung as it lay on the mediastinum

Case 2 A Msutu boy, aged 3, suffered from coarctation of the aorta He had had four episodes of left ventricular failure with triple rhythm, an alternating pulse (10 mm of mercury) and moist sounds in the lungs, but when admitted his general condition was fairly good and failure had cleared apart from some rales in the left lung Both carotids were pulsating vigorously, and the apex beat was in the sixth left interspace in the anterior axillary line The femoral pulses could not be felt A systolic murmur was heard over the third left interspace just lateral to the sternum The blood pressure was 110/90 in the left arm and 170/120 in the right There was some retarded development of the buttocks and legs

X-ray examination confirmed the enlargement of the left ventricle and showed a normal aortic knuckle, but also slight enlargement of the right ventricle There was notching of the ribs on the right side though not on the left The following suggestions were made to account for his right ventricular enlargement

(*a*) A patent interventricular septum, but the murmur was atypical

(*b*) A co-existing patent ductus arteriosus without the characteristic machinery murmur In view of the child s age it was difficult to dismiss this possibility, which would imply that the coarctation was infantile in type with a wider area of stenosis than usual This was supported by the absence of notching of the left ribs

(*c*) The four previous attacks of left-sided heart failure had resulted in hypertrophy of the right ventricle The pulmonary vascular X-ray shadows were noted to be heavy

Induction of a pneumothorax followed by screening and, if necessary thoracoscopy presented itself as the simplest means of deciding, and was performed on the left side with 500 ml of air Screening showed that the lung was partially collapsed and, with the child vertical, was falling away from the mediastinum The aortic knuckle pulsated vigorously but seemed to be cut short about the middle of the arch Three days later a thoracoscope was inserted in the 4th left interspace between the scapular border and the spine the patient lying on his right side Because the lung overlay the

mediastinum the patient was then turned on his left side, and the table tilted into a moderate counter-Trendelenburg position The view now obtained through a right angle vision telescope had completely changed the lung had fallen outwards, downwards and forwards, putting the pulmonary hilus on a slight stretch (Fig 1) The aortic arch was well exposed as it emerged from under the thymus, and the descending aorta could be viewed from above for a considerable part of its length towards the diaphragm A tight coarctation was identified involving the root of a very small subclavian artery and extending for about 1 cm outwards The descending aorta was pulsating less than the arch above the coarctation, and there was less discrepancy between the calibre of the aorta distal and proximal to the coarctation than had been expected Several large upper intercostal vessels were seen, and also a large internal mammary artery The vasa vasorum on the descending arch just distal to the constriction were dilated A good view of the surface of the lung hilus was obtained No ductus arteriosus was visible nor fold of pleura raised by a ligamentum arteriosum The lung and descending aorta appeared normal After withdrawing the telescope air was sucked out of the chest and the wound closed with a stitch The child slept for six hours following this procedure but next day developed a consolidation of the middle lobe of the right lung, from which he made an uneventful recovery However, at operation one month later he died after the chest was opened and before the coarctation was excised The heart stopped beating and could not be made to contract again Postmortem the heart weighed 121 grams, showing marked hypertrophy of the left ventricle and, to a less degree, of the right ventricle There was no patent ductus arteriosus The coarctation was confirmed at the level of the root of the atresic subclavian artery Microscopic examination showed extensive perivascular fibrosis of the myocardium and intimal plaques of calcium in the coronary arteries

Case 3 A European boy, aged 7, suffered from Fallot s tetralogy He had been blue since the age of one year and cyanosis was increased by exertion He could not run at all fast and after ambling for about 30 yards he would squat on his heels

On examination the veins of the neck were engorged above the angle of Lewis The fingers were clubbed and the nails were cyanosed as was the face even when at rest in bed Arterial pulsation was visible above the clavicles The apex beat was within normal limits, but there was a heaving impulse over the præcordium A systolic murmur was present over the whole præcordium loudest over

the second left intercostal space   There was no enlargement of liver or spleen   Blood pressure 110/90 in both arms   The red cell count was 7,100,000   X-ray examination showed right ventricular enlargement with the aortic knuckle on the left   The pulmonary conus was visible but diminished on its under side   The pulmonary vascular shadows were slight, especially towards the lung periphery   There was right axis deviation

A right pneumothorax was induced with 400 ml of air and a thoracoscope (Coryllos-direct) was inserted into the first right intercostal space in the midclavicular line   The subclavian artery was well

difficulty in performing the anastomosis and this was confirmed by immediate thoracotomy on the right side

Case 4   A Zulu girl, aged 9, was admitted in congestive heart failure   No good history could be obtained and it was impossible to find out whether she had ever suffered from rheumatism or not   The veins of the neck were engorged and pulsating two inches above the angle of Lewis   She had œdema of both ankles and an enlarged liver but was not unduly breathless when lying in bed, but stated she was breathless when on her feet   Blood
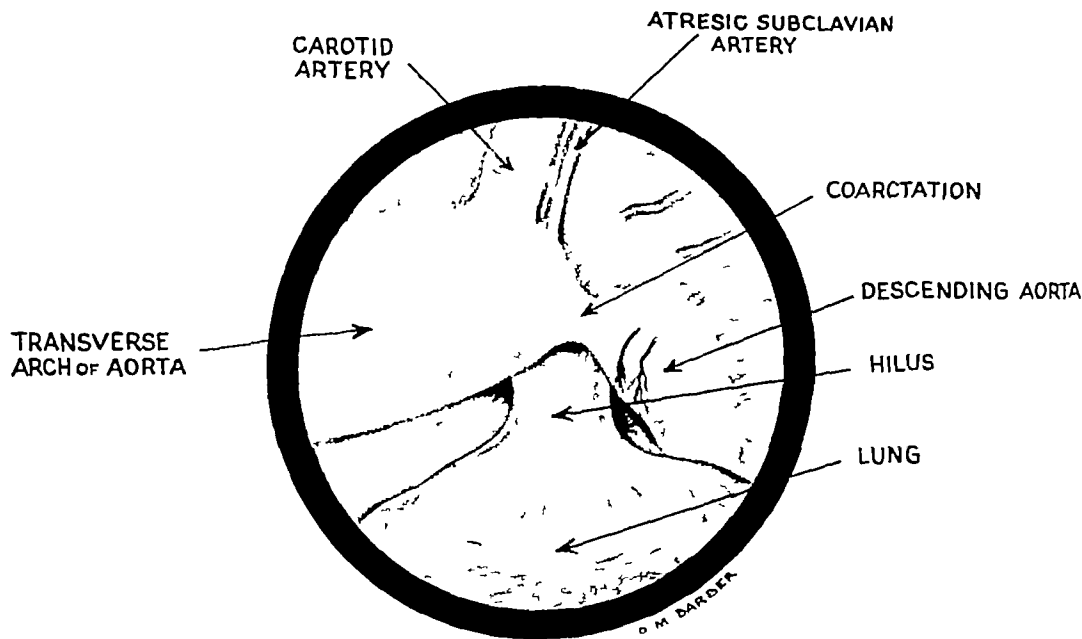
Fig 1 —Case 2   Aortic arch seen from the side and above by right angled telescope

visualized and also a considerable number of collateral vessels   The subclavian appeared to be a large artery and raised a ridge on the mediastinal pleura   A large innominate vein was seen with a vein running from it to communicate with a large azygos   The pulmonary artery could not be identified because of numbers of small engorged veins just above the hilus of the lung and the azygos vein   Although the pulmonary vessels could not be seen their position was estimated approximately from the level of the hilar pleura   The aortic arch was viewed travelling towards the left and not descending on the right side   The appearance of the subclavian artery suggested that there would be no

pressure 104/60   Pulse regular 144   The apex beat was in the 5th space just outside the mid clavicular line   The præcordium was bulging and a diffuse heaving impulse was visible, with an apical systolic thrill   There was a harsh systolic murmur loudest over the apex but audible over the whole præcordium   In the 2nd left interspace an inch outside the sternal margin, there was also a sound that at times seemed to fill the whole diastolic pause, but because of the tachycardia it was difficult to decide whether this was really a machinery murmur or a third closed sound   Phonocardiography did not help   After a week s treatment with digitalis she came out of failure but her pulse rate never came

down below 120   X-ray examination and screening revealed a mitral-shaped heart, considerably increased in its transverse diameter   Both ventricles were enlarged, the right more than the left and also the left auricle   The aorta appeared to be hypoplastic   There was some vascular congestion of both lung fields but no hilar dance   Various diagnoses were considered

Cardiac catheterization (Dr van Lingen) gave no evidence of an intracardiac vascular shunt   The catheter point failed to pass into the pulmonary valve and appeared to be washed back from it, which was regarded as evidence of pulmonary incompetence   However, in spite of the atypical X-ray and blood pressure we decided, in view of the

child developed acute nephritis and operation has had to be deferred   Her heart rate is slower and the murmur is now typically machinery in character

Case 5   A European boy, aged 9, was sent in as a case of coarctation of the aorta   The blood pressure in both arms was 150/120 and his femoral pulses could not be felt   His condition was complicated by petit mal   He was otherwise a bright and normal boy   It was decided to control the petit mal with phenobarbitone before operating and to perform thoracoscopy with the idea of not only viewing the coarctation but of assessing any change in the condition of the aorta that might occur subsequently
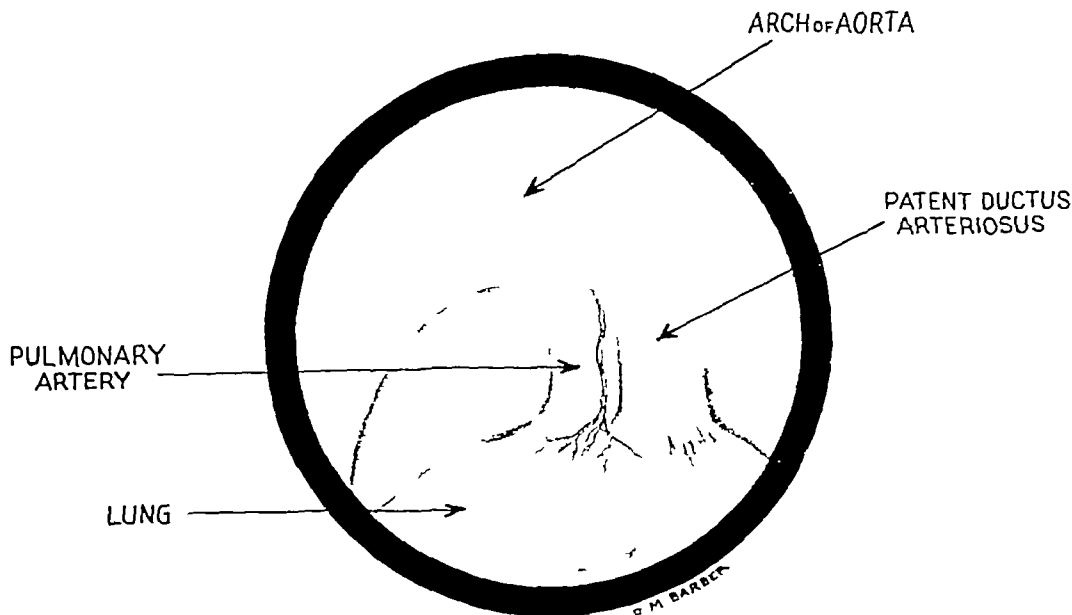
Fig 2 —Case 4   View of aortic arch and lung root seen from above   Distorsion of the aortic arch is due to the proximal part to the left being closer to the telescope than the other end

very suggestive murmur, to attempt to exclude a patent ductus by means of thoracoscopy   Accordingly, a left pneumothorax was induced and a thoracoscope introduced by a posterior approach in the 4th left interspace close to the scapula with the child lying on her left side   This gave a good view of the hilus, and showed a large vessel underneath the aortic arch in close contact with it (Fig 2)   It was, however, difficult at the time to establish whether this was a patent ductus or the pulmonary artery   Its apparent origin from the anterior surface of the aortic arch strongly suggested a ductus and in the light of further experience we are now convinced that this was so   Meanwhile the

A left pneumothorax was induced with 400 ml of air and the thoracoscope was inserted immediately, using the anterior approach in the 2nd left interspace in the midclavicular line   An excellent view was obtained with the direct and also with the right-angled telescope   The coarctation was seen to be about a quarter of an inch long and slightly less in its outside diameter   The transverse aortic arch was dilated   Dilated subclavian and internal mammary arteries were clearly visible (Fig 3)   Unexpectedly a patent ductus arteriosus was seen arising close to the beginning of the coarctation clearly separated from the pulmonary artery by a gap and having a lymph gland overlying it   A small

2c

vascular leash crossed over the ductus arteriosus
The vagus nerve, flanked by small arteries, hooked underneath and disappeared behind the hilus
The objective lens of the telescope could be brought into contact with the duct and its impulse with no thrill was easily felt on the shank of the thoracoscope
This manœuvre caused some discomfort to the patient The ductus was wide and appeared to dilate aneurysmally with each pulsation This patient is now awaiting operation, which seems imperative owing to risk of rupture of his aorta,

enlargement, no thrill A soft machinery murmur was heard in the 2nd left intercostal space audible also at the vertebral border of left scapula in 2nd and 3rd interspaces Blood pressure 150/60 *Femoral pulse easily palpable*

A left pneumothorax was induced with 600 ml of air The thoracoscope was introduced immediately through an anterior approach in the 2nd left intercostal space in the midclavicular line A very blue pulsatile pulmonary artery was seen with an almost orange coloured ductus arteriosus rising
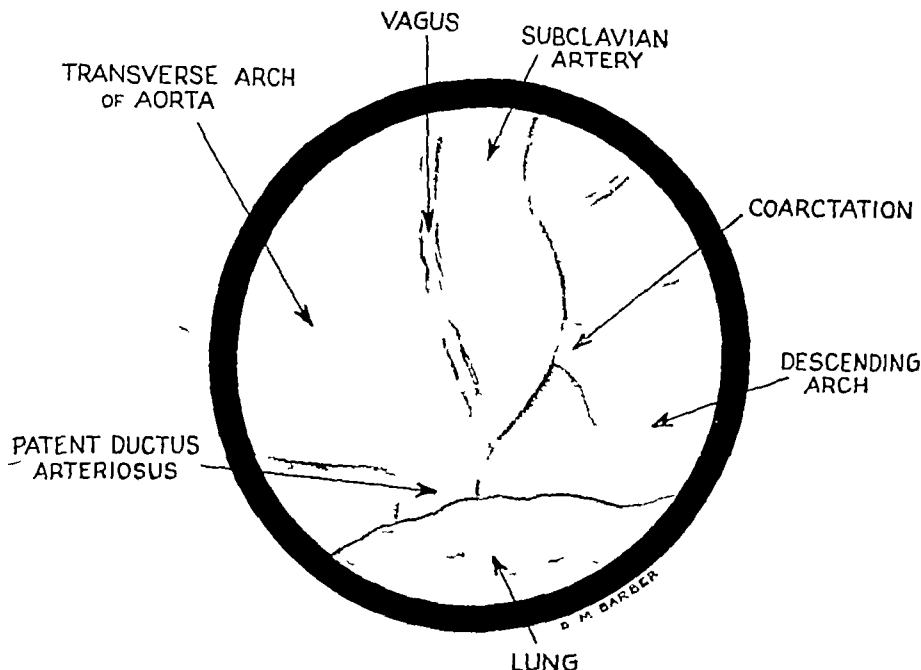
FIG 3 —Case 5 The aortic arch seen from the front and above The proximal aorta was greatly dilated and overlay the beginning of the coarctation The vagus and its accompanying small vessels were more visible than usual

the proximal part of which is very dilated The ductus arteriosus will be ligated at the same time At the moment he is undergoing treatment to control *his epilepsy*

Case 6 A woman, aged 21, noticed no symptoms as a child, but a ' machinery murmur was heard at the age of 9, and for this reason she was refused life assurance a few months ago For the past three years she has been listless, tired, breathless on exercise, and dizzy on bending She is due *to get married shortly*

On examination, slight pulsation in the neck and second left intercostal space, no clinical cardiac

from the antero inferior aspect of the aortic arch (Fig 4) Pulsation of the ductus was less than that of the pulmonary artery A small arterial leash was visible on the surface of the ductus with two small lymphatic glands along side The aorta appeared to be somewhat angulated just proximal to the ductus but was otherwise normal Operation performed on the following day confirmed these findings but, in addition revealed a very slight indentation of the aorta just proximal to the ductus at the site where an infantile coarctation occurs A very marked systolic thrill was palpable in the ascending arch up to the site of the constriction By auscultation before and after ligation and

division of the ductus we both confirmed the disappearance of the murmur after ligation Two days after operation it had returned, and this was confirmed when seen again one month later

Case 7 A European male, aged 19, complained of slight blueness and dyspnœa, both aggravated by exercise, occasional slight giddiness on exercise, and some palpitation His mother noted cyanosis at birth, aggravated by crying He had been difficult to rear, but had suffered from the usual children's

marked in the lips, tip of nose, lobes of ears, fingers, and toes Eyes suffused and marked clubbing of fingers No venous engorgement in the neck Blood pressure, right arm 125/60, left arm 115/60 No abnormality or evidence of congestion found in the lungs Apex beat forcible and diffuse within the mid-clavicular line and in the 5th and 6th intercostal spaces At the base of the heart there was a mild thrill with a loud systolic murmur in the second left space this murmur was localized, but a softer systolic murmur was heard over the rest of
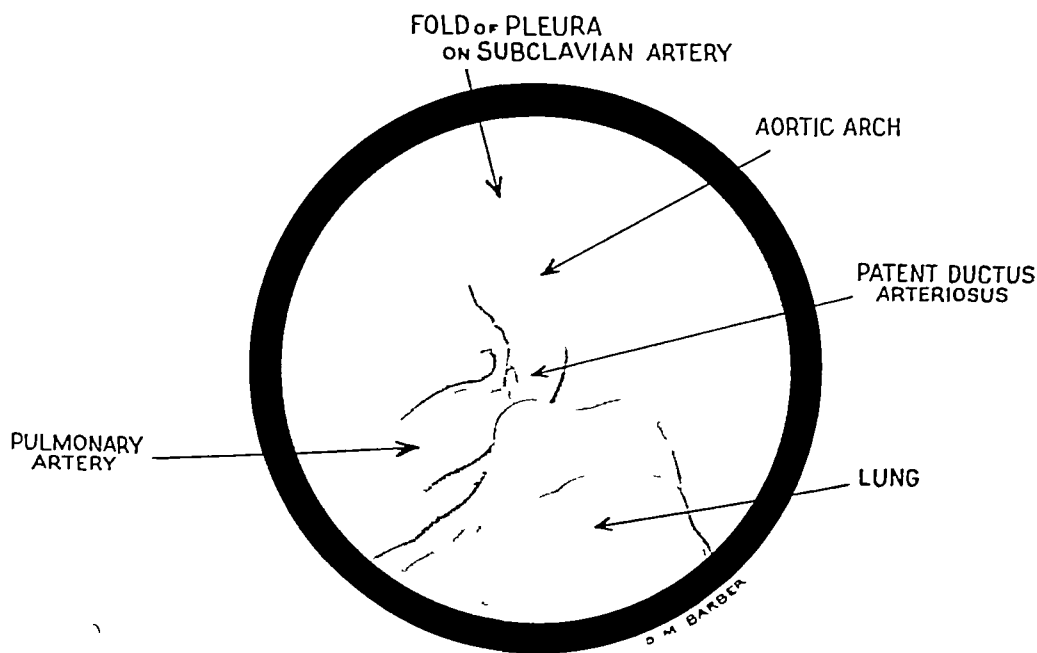
FIG 4 —Case 6 Aortic arch and lung root seen from the front and above
The arch is more acutely angled than usual

diseases, including whooping cough, without trouble Walking was delayed until after the third year No other members of the family suffered from congenital defects, his mother had been healthy during pregnancy and the labour had been normal

Although early growth was retarded his height is 5 ft 11 in and weight 117 lb His present activity is restricted to walking on the flat without hurrying Cyanosis, which is minimal at rest, becomes pronounced on moderate exercise and during extremes of weather Squatting is not marked, but he adopts a knee-chest position for comfort when fatigued The parents think he has improved during recent years and are interested in the possibility of a Blalock-Taussig operation

On examination, slight generalized cyanosis more

the præcordium The second sound was closed and much accentuated in the 2nd left intercostal space Radioscopy showed some cardiac enlargement predominantly right ventricular, although the left ventricle was also enlarged to a lesser degree The aorta pulsated vigorously In the antero-posterior view the pulmonary conus was slightly prominent and not concave, but the left oblique view suggested that the pulmonary artery was small Despite the prominence of the lung markings no pulsation was seen A barium swallow showed the aorta to arch downwards on the left side The X-ray evidence favoured Fallot's tetralogy with a good collateral circulation through a patent ductus or bronchial arteries, it did not suggest Eisenmenger's complex Venous catheterization of the heart (Dr van Lingen)

2c*

demonstrated the ventricular septal defect by passing the catheter through it, and analysis of blood samples suggested a right to left shunt An overriding aorta was demonstrated with reasonable certainty by the fact that the oxygen content of the left ventricular blood was higher than that from femoral artery puncture Failure to record pressures in the pulmonary artery or to obtain equal systolic pressures in the aorta and right ventricle precluded differentiation between Fallot's tetralogy and an Eisenmenger complex The final diagnosis

colour and slightly tortuous, which entered the hilum as a network and almost hid the pulmonary artery A few enlarged vessels were to be seen on the lung surface In the angle between the subclavian artery and the curve of the arch another and thicker plexus of dark vessels was seen, presumably collaterals of the intercostal arteries dipping under the arch to enter the hilum The vessels on the surface of the aortic arch numbered about 25, extending from the ascending aorta over to the descending, many more than would be expected from
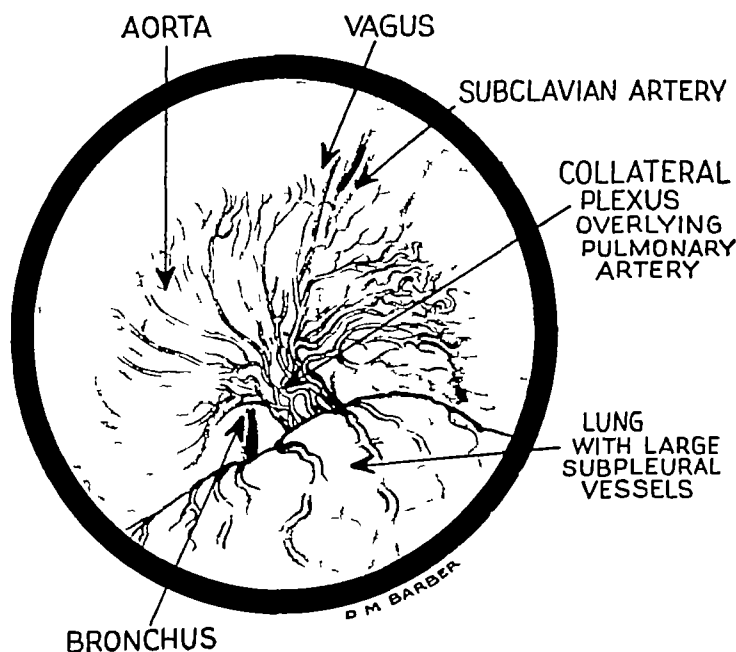
FIG 5 —Case 7 The aortic arch seen from the front and above Note the plexus of collateral vessels crossing the aortic arch to reach the hilum and overlying the pulmonary artery The arrows indicating the vagus and the bronchus are a fraction too far to the left

was Fallot's tetralogy with a possible patent ductus arteriosus or a collateral circulation to the lungs by bronchial arteries

It was decided to submit this case to thoracoscopy in order to determine what form of collateral circulation was present and also, if possible, to take the pressure in the pulmonary artery by means of a needle introduced and withdrawn under direct thoracoscopic vision A pneumothorax was introduced with 400 ml of air, and the thoracoscope inserted in the 2nd left interspace in the midclavicular line, the patient reclining at an angle of 45° to the horizontal The aortic arch was immediately seen, and presented a remarkable picture (Fig 5) being crossed radially by numerous vessels, dark blue in

bronchial arteries alone and some seemed to come from the enlarged internal mammary artery The pulmonary artery was small, and through another cannula, about an inch lateral to the first a long needle was inserted into its small exposed part The systolic pressure, read on a saline-citrate manometer, registered 20 cm above the manubrium (normal 25 cm) On removing the needle only a few drops of blood were seen and, when washed off with saline, did not reappear Air was aspirated from the chest, the cannula removed and the wounds closed with one Michels clip each No untoward effects were noted by the patient, nor had any sensations been felt during the needling of the vessel

The thoracoscopic finding confirmed that the collateral supply to the lung was good, though not provided by a ductus arteriosus It also showed that, although the pulmonary artery was small, the extensive collaterals were enough to raise its pressure even at the hilum to four-fifths of the normal, and that it is easier to obtain the pulmonary arterial pressure by this method than by cardiac catheterization in cases of narrowing of the pulmonary infundibulum or valves

On the reasonable assumption that a similar collateral supply was present on both sides of the aortic arch, it was thought wiser not to perform Blalock s operation on this patient

ANÆSTHESIA AND TECHNIQUE

In adults, local anæsthesia is the anæsthetic of choice, with omnopon, one-third of a grain, given an hour before With suitable doses of omnopon the same anæsthesia applies to children down to the age of 7 or 8 years Below this age, various types of general anæsthesia are used with equal success, and we have successfully given intravenous nembutal, or cyclopropane and oxygen after a basic narcotic of seconal, or ether by the closed method after a similar basal narcotic Insufficient narcosis causes difficulty from restlessness and irregular movements of the chest, as the child is too unconscious to co-operate and not deep enough to be quiet Even trilene anæsthesia is fairly satisfactory in spite of the rapid breathing if a large enough pneumothorax is induced In children of five to eight years, 400 to 500 ml of air can be introduced without distress

The procedure of thoracoscopy need not be enlarged upon, as its technique is well known, but a few special points are worthy of mention The pneumothorax is induced in the operating theatre, immediately before the operation, unless the lung is expected to be adherent, when the induction is done under an X-ray screen a day or two before If there is widespread adhesion this method of investigation must of course be abandoned

After trying various sites of introduction we have found the most satisfactory approach to be the anterior, in the second interspace in the mid-clavicular line, with the table tilted to an angle of about 45° in the counter-Trendelenburg position A lateral tilt may be added, but is only occasionally necessary, if the greater part of the descending thoracic aorta is to be seen For the visualization of a coarctation or of a patent ductus the direct telescope gives the best view, this should, however, be supplemented by the right-angled view, especially if the thymus or the internal mammary artery are to be seen The subclavian artery in Fallot's tetralogy is better seen with a right-angled telescope but

the direct telescope should also be available in order to obtain as good a three-dimensional idea as possible When investigating coarctation, it is as well to insert the trocar and cannula as nearly as possible in the centre of the intercostal space to avoid both an enlarged intercostal artery and its anterior branch running along the upper border of the rib below, in practice, we have not met with this complication

Any thoracoscope with direct and right-angled telescopes can be used, the 9-mm Gullbring type as modified by the Genito-Urinary Co has been very satisfactory, the 7-mm Coryllos type gives a smaller field which is its only disadvantage Oxygen can be given during the investigation, but is usually unnecessary even with cyanotic children, unless a very large collapse of the lung has been produced The major operation can be proceeded with immediately, as was done in Case 3, no harm seems to have accrued from this, nor is it to be expected

DISCUSSION

We believe that thoracoscopy is a useful diagnostic procedure in certain congenital abnormalities of the great vessels and may give information that cannot be gained by X-ray examination even with the use of radio-opaque substances The injection of these substances into the basilic vein often gives unsatisfactory results and when they are injected into the right auricle there is an appreciable risk to the patient's life, which is absent when the alternative procedure of thoracoscopy is employed

As was only to be expected the hilar structures cannot always be visualized distinctly but, on the other hand, the gap to be bridged between the aortic arch and the pulmonary artery can be estimated fairly accurately This was so in Case 3, where the pulmonary vessel was covered by a thick network of collateral veins and the artery could not be seen, though its position could be assessed with reasonable accuracy In patent ductus arteriosus our experience indicates that an anterior approach gives a better view of the anatomy than a posterior and, while we would hesitate to claim that in cases in which no ductus can be seen its existence is excluded, we would emphasize that when a patent ductus is visualized it is unmistakeable

In Case 4, the posterior approach was used and, although a structure was seen originating from the anterior aspect of the aortic arch the limited field of vision made it impossible to be certain that we were not looking at the pulmonary artery itself In the light of our later experiences with Cases 5 and 6 we now feel convinced that this was a patent ductus

In childhood before the typical machinery murmur of patent ductus has developed there seems to be

some value in thoracoscopy to differentiate it from other conditions, especially auricular septal defect This difficulty was noted by Taussig (1947) who stated " in infancy there is nothing in this age group to differentiate this murmur from the systolic murmur associated with the patent ductus arteriosus or one caused by ventricular septal defect " There appears to be a place for thoracoscopy here If the ductus is short it is more difficult to see than if it is long, and a " keyhole " ductus is almost certainly invisible

The arch of the aorta can be viewed clearly and in coarctation the constriction can be seen and its extent estimated, one can also make sure that the calibre of the vessel distal to the coarctation is such that it can be anastomosed to the proximal segment These items of information are difficult and usually impossible to obtain by X-ray methods and angiography Crafoord (1945) reported two cases that were found inoperable at thoracotomy, and others have undoubtedly occurred

Blalock (1946 and 1948) stipulates that a low pressure must be found in the pulmonary arteries before his operation is indicated In doubtful cases in which a catheter cannot be passed through the pulmonary valve a thoracotomy is necessary to obtain this reading As is demonstrated in Case 7 it may be possible to insert a needle into the pulmonary artery under view through the thoracoscope and thus obtain the pressure reading This may not always be possible owing to anatomical varia-

tions but we claim that if thoracoscopy is practised as a routine investigation in these cases some thoracotomies may be obviated

It is not always easy to diagnose the condition of double aortic arch or to differentiate the various types of anomaly involved Sweet et al (1947) describe a case in which the aortic arch was thought to be right sided, with a left-sided arch compressing the trachea, a left thoracotomy showed that the major arch was in fact left sided, but passed behind the œsophagus into the right thoracic cavity, where it was joined by a small right arch which produced the compression A subsequent right thoracotomy enabled them to divide the right arch and effect a cure Preliminary thoracoscopy in this type of case would enable a more accurate diagnosis to be made before operation, though here the procedure would have to be bilateral

CONCLUSIONS

The technique of thoracoscopy as an aid to diagnosing certain congenital cardiac conditions has been discussed

Seven cases are described in which this procedure was employed The scope and limitations of this method have been briefly discussed

We wish to thank Professor G A Elliott Witwatersrand University, for permission to publish Case 7 and Dr S Selby, Coronation Hospital for Case 2
We are indebted to Dr J L Lovibond for much helpful criticism, and to Miss D M Barber for the drawings

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PROCEEDINGS OF THE BRITISH CARDIAC SOCIETY

The THIRTEENTH ANNUAL GENERAL MEETING was held at Newcastle, Co Down, Northern Ireland, on Thursday, June 2, 1949

Chairman S BOYD CAMBELL

The Chairman took the Chair at 10 a m , 74 members and 17 visitors were present

PRIVATE BUSINESS

1 The minutes of the last Annual Meeting, having been published in the Journal (10, 293, 1948), were taken as read and confirmed

2 The balance sheet for 1948–49 was presented, having been audited and found correct by Bedford and Maurice Campbell The credit balance on April 30, 1949, was £85 18s 5d

3 Lovibond and Bruce Perry were elected members of the Council in place of Brown and Cotton (terms of office expired)

4 Fraser and Hope Gosse were elected *Extra-Ordinary Members*

5 The following Associate Members were elected as *Ordinarv Members*

D R Cameron, W J Cooke, R J Duthie, Frances Gardner, G W Hayward

6 The following new *Associate Members* were elected

J Benn, Bristol
W W Brigden, London
T H Crozier, Belfast
R Daley, London
Courtenay Evans, London
C J Gavey, London
G A Kiloh, Chester
R Kauntze, London
A Leatham, London
J W Litchfield, London
D C Muir, Hull
D A Robertson, London
A J Thomas, Cardiff
B G Wells, London

7 The following *Associate Members* were elected for a further period of three years

R Kempthorne   C G Parsons
D Lewes   W K Stewart
C Papp   W Stokes

8 The following alteration was made in Rule 22 " The subscription shall be fixed by the Council and shall not exceed two pounds a year for Ordinary Members and one pound for Associate Members, it shall become payable on the 1st day of March Failure to pay the subscription due within two years shall be considered equivalent to resignation "

9 It was decided that an Autumn Meeting should be held in 1949 and that the Council should determine the date and the place of the meeting

10 A memorandum by the Honorary Secretary on the International Council of Cardiology was considered It was agreed that it should be left to the Council of the Cardiac Society to nominate a delegate and a deputy to the projected meeting of delegates to be held in Paris in 1950 It was agreed, at the suggestion of Bain, that there should be adequate representation of the British Commonwealth at the meeting of delegates

11 A recent meeting of delegates to form a European Society of Cardiology was reported and some observations on this were made by the delegate of the British Cardiac Society, Evan Bedford At the suggestion of Chamberlain, the Council was asked to consider whether or not the German Cardiac Society should be allowed to join the European Society of Cardiology

DISCUSSION ON RHEUMATIC HEART DISEASE

Opening speakers
(i) Ætiology of Rheumatism
    (a) Public health A C Stevenson
    (b) Pathology J H Biggart
(ii) Rheumatic Heart in Pregnancy
    (a) Clinical aspects Robert Marshall
    (b) Pathology Florence McKeown

A C STEVENSON (*introduced*) There is need for further illumination of the epidemiology of rheu-

matic fever, at times too sweeping deductions are made from the rather scanty data referring to juvenile rheumatism and its sequalæ Certain limits can not safely be passed in interpreting the mortality figures of the Registrar General relating to acute rheumatic fever and heart disease Moreover, little information is available from the School Medical Service and from notifications and planned enquiries pursued over a long period from rheumatism clinics seem likely to be the most fruitful

source of information   Some figures are available relating to patients attending the clinic at the Royal Belfast Hospital for Sick Children

Hypotheses concerning the relationship of streptococcal infections to juvenile rheumatism are based on scanty data   The conception of rheumatic fever as the end stage of a post-streptococcal state is interesting and attractive but does not appear to be based on much recorded observation   The evidence of familial susceptibility, as advanced most convincingly in recent years by Dr May Wilson, of Cornell, has not received sufficient attention and even if the proposition of hereditary transmission of susceptibility by a single autosomal recessive gene is difficult to support, there is overwhelming evidence of some inherited susceptibility

J H BIGGART (*introduced*)   In spite of much research, the ætiology of rheumatic fever remains undiscovered   Theories involve the streptococcus pyogenes, streptococcus viridans, a specific streptococcus, or viruses, but the evidence necessary to establish any one of these is still lacking   The work of the German School has produced the theory of an allergic mechanism as the responsible factor

Difficulties arise in accepting such an allergic hypothesis—the granulomatous character of the essential lesion, the limitations of its distribution to the cardiovascular system, the specific sites for its occurrence, and its specific life-history   In addition to such purely morphological reasons for challenging the allergic hypothesis, there is the clinical suggestion of the importance of upper respiratory infection as a precursor of the rheumatic attack

Study of the lesions produced in the rabbit by serum hypersensitivity shows that many of these difficulties can be overcome   The granulomatous lesion, the specific distribution, etc , are duplicated in the experimental animal   It is therefore suggested that no matter what the ætiological agent of rheumatic fever it produces the specific histological picture through an allergic mechanism

ROBERT MARSHALL (*introduced*)   In spite of the steady fall in maternal mortality during the past 15 years, heart disease was actually gaining a more prominent position as a cause of maternal deaths During the quinquennium 1943–47, 743 women in England, Wales, Scotland, and Northern Ireland have died from heart diseases associated with pregnancy and childbirth   The commonest lesion was mitral stenosis, a fact borne out by the figures collected by Kenneth Hudson from the Royal Maternity Hospital, Belfast, where in the years 1937–48 there were 24,078 total admissions, with

an incidence of 1 8 per cent of heart disease, and a maternal death rate from this cause of 5 8 per cent, this compares with MacRae's findings in Queen Charlotte's Hospital, where the incidence was 0 8 per cent and the maternal death rate 3 1 per cent among 29,713 admissions   In Belfast 76 per cent of the deaths were emergency admissions, and 50 per cent occurred in connection with the patients first pregnancy   These figures are comparable with those of Bramwell and Longson in Manchester, Carr and Hamilton in Boston, and Watson in New York

The ætiological factor was rheumatic fever in 40 per cent of cases, and chorea in 12 per cent   A history of " ambulatory " pains was given in 15 per cent, but 22 had no history of relative disease Mitral stenosis was diagnosed in 85 per cent of cases   It is of great importance to search carefully for this lesion during the ante natal examinations, in order to eliminate admission to hospital of patients as " emergencies " with a high risk of death   As MacRae has stated, changes in the heart and circulation in pregnancy may cause breathlessness and palpitation, even in healthy patients,   thus the cardinal signs of early congestive failure are rendered the more difficult to assess   Perhaps the most useful clinical hint is given by determining what number of pillows the patient requires at night If signs of congestive failure are suspected during pregnancy, the patient should be admitted to hospital for a period of rest and observation, and all heart cases should be admitted at least a week before the date of expected confinement   While Caesarean section might still be advisable for cardiac, as well as obstetric, reasons, the practice of induction of labour for cardiological reasons has fallen into disrepute among obstetricians

A series of 150 hospital in patients during the years 1942–1946 has been reviewed   Of these, 8 are known to have died, and 36 have not yet been traced for various reasons   Of the first 100 patients reviewed, the ætiological factors and cardiac lesions corresponded closely with the larger series   Forty patients had been aware of cardiac symptoms during their first pregnancy, but 34 had developed such symptoms during their first pregnancy   Of these, 20 had suffered from rheumatism or chorea, but 14 had had no reason to fear heart disease, which was an additional argument for careful search for evidence of mitral stenosis at all ante natal examinations   Five women had expressed the opinion that their health was better than before their confinements, 42 were thought to be unchanged, but 53 considered that their health had been impaired by pregnancy and parturition   It has to be remembered that it is not enough to nurse one s patient with mitral stenosis until her baby is safely

born, but that child-bearing is a prelude and a part of child-rearing

FLORENCE MCKEOWN (*introduced*) A post-mortem analysis is presented of 9 cases of rheumatic heart disease complicating pregnancy In 3 of these the strain of pregnancy was the apparent cause of decompensation The mechanism of heart failure in these cases is debatable, but stress must be laid on the lesions of the coronary arteries which result from previous attacks of rheumatic carditis and appear to play an important part in lowering the cardiac reserve

In the remaining 6 cases a recrudescence of rheumatic fever, which was usually sub-clinical, was responsible for decompensation Sub-clinical rheumatism is of importance in relation to pregnancy, but only by routine post-mortem examinations, which should include histological study of many blocks of the heart, can the occurrence of such attacks be recognized

The opening papers were followed by a discussion to which contributions were made by Bramwell, East, Gilchrist, Schlesinger, Bain, Abrahamson, and Crozier

<div style="text-align: center">SHORT COMMUNICATIONS</div>

VENTRICULAR SEPTAL DEFECT IN EARLY CHILDHOOD

BY A RAE GILCHRIST AND ROBERT MARQUIS (*introduced*)

Although an isolated defect of the ventricular septum is recognized as one of the less serious congenital malformations of the heart, autopsy reports suggest that such a lesion is more frequently responsible for death in early childhood than is generally appreciated Of Maude Abbott's 50 cases, 21 died at five years of age or under In 110 consecutive cases of congenital heart disease coming to autopsy at under three years of age in the Edinburgh Royal Hospital for Sick Children, a defect of the ventricular septum, without other gross malformation of the heart, was found in approximately 25 per cent In this group the predominant cause of death was an associated respiratory infection, but in a small proportion the death was primarily due to heart failure

It is suggested that the differential diagnosis of congenital heart disease in young children must include the isolated ventricular septal defect, even when the disability is gross In support of this contention 4 cases are presented They conform to a general pattern of which the principal features are under development from an early age, an absence of cyanosis, a liability to respiratory infections, and a tendency to congestive heart failure The heart is enlarged, a loud systolic murmur is maximal up the left sternal margin, and the pulmonary second sound is accentuated The electrocardiographic tracings are bizarre but suggest hypertrophy of both right and left ventricles Radiological examination confirms this enlargement and shows the pulmonary artery to be enlarged and the hilar shadows to be prominent

Autopsy findings are given in two of the cases

presented Both show defects of the ventricular septum, in one the defect replaces the membranous septum, in the other the anterior part of the muscular septum is also involved The pulmonary artery is larger than the aorta and there is right and left ventricular hypertrophy in both specimens Other changes are minimal

APICAL DIASTOLIC MURMURS IN PERSISTENT PATENCY OF THE DUCTUS ARTERIOSUS

BY FRANCES GARDNER AND M ZOOB (*introduced*)

A diastolic murmur was audible at the cardiac apex in 9 patients with patent ductus arteriosus and was recorded phonocardiographically In 5 patients the murmur could not be distinguished from the diastolic component of the Gibson murmur In 4 a mid-diastolic murmur, resembling that of mitral stenosis was present, and in two of these the mid-diastolic murmur disappeared after ligation of the ductus, and in a third autopsy showed no stenosis of the mitral valve

Phonocardiographic evidence suggested that the murmur did not represent transmission of the Gibson murmur to the apex It was found that the maximum intensity of the Gibson murmur corresponded with the period of relative quiet between the second sound and the mid-diastolic murmur Furthermore, it was found that respiration produced opposite effects on the two murmurs The mid-diastolic murmur was increased during inspiration This would be expected if it were dependent upon flow through the mitral valve The Gibson murmur was diminished during inspiration

It is concluded that the murmur belongs to the group of functional mid-diastolic murmurs and that it is not necessarily evidence of mitral stenosis in the presence of patent ductus arteriosus

An Apparatus for Intermittent Venous Occlusion

By J Shillingford (*introduced*)

Over ten years have elapsed since Collens and Willensky described their results of the treatment of peripheral vascular disease by intermittent venous occlusion   They showed that this method of treatment was capable of relieving pain, healing ulcers, and increasing walking capacity

Since this time somewhat conflicting reports have been received as to the value of this method, but there seems little doubt that, clinically, a proportion of patients with peripheral vascular disease are greatly benefited by continued intermittent venous occlusion

To date, there has not been generally available a simple, and portable, machine suitable for hospital and home use   An apparatus, which will shortly become generally available, has been designed and is now demonstrated   It is small in size, portable, silent in operation, with few moving parts, and can be worked by the patient himself with the minimum of instruction   Any convenient electric light point can be used as its source of power

Diagnostic Problems in Congenital Cyanotic Heart Disease

By Violet Breakey (*introduced*)

Two cases illustrating diagnostic problems in congenital cyanotic heart disease were discussed in detail

(1) pure pulmonary stenosis, and

(2) pulmonary tuberculosis occurring in association with the tetralogy of Fallot

The first case at autopsy showed a stenosis of the pulmonary valve with intact ventricular septum and widely patent foramen ovale   The significant clinical features distinguishing the case from the classical tetralogy of Fallot appeared to be

(1) The age of onset of cyanosis was much later, 1 e not until five years,

(2) dyspnœa was out of proportion to cyanosis, but attention was drawn to the fact that there were some patients with the tetralogy of Fallot who maintain a relatively high arterial oxygen at rest but rapidly become anoxæmic on the slightest exertion,

(3) cyanosis appeared to vary even more than in the usual tetralogy of Fallot, and

(4) the cardiac contour was strikingly different, with notable fullness of the pulmonary artery and of the right auricle   However, there was not the gross right ventricular enlargement that might be expected

The choice of surgical procedure in such cases with a tissue-paper thin pulmonary artery was an important matter

The importance of lung shadows in congenital cyanotic heart disease was mentioned   Rokitansky stated in 1866 that pulmonary tuberculosis and pulmonary stenosis were incompatible   However, textbooks continued to teach that phthisis was a common cause of death in pulmonary stenosis, presumably arguing from the false premise that pulmonary tuberculosis was rarely seen in the vascular lung of mitral stenosis   It seemed now, however, that pulmonary tuberculosis was in fact exceedingly rare in the presence of pulmonary stenosis   In the second case a low pulmonary blood flow consequent on pulmonary stenosis resulted in an unusual picture—a relative absence of toxicity and progression during 12 months in spite of wide spread infiltration

Cardiac Catheterization in Congenital Heart Disease

By G J Aitken

The author presented tables illustrating the results obtained from cardiac catheterization in 20 cases of congenital heart disease   The findings agreed with those reported in other series   Particular reference was made to the relative proportion of successful catheterizations of the various cardiac chambers   An unusual course was not infrequent, the most common being into the coronary venous sinus and middle cardiac vein   Such courses were described

Complications and technical difficulties were discussed   With one exception, venous spasm had been easily controlled   Abnormalities of rhythm were noted in 9 cases   In 8 this took the form of isolated extrasystoles occurring during intracardiac manipulation of the catheter   In the remaining one catheterization initiated a paroxysm of auricular fibrillation, which was terminated by quinidine when early signs of acute congestive failure appeared   Venous thrombosis, apart from a little about the point of entry of the catheter, has not been encountered   In one patient who died of congestive cardiac failure 14 days after catheterization, no evidence of intravascular trauma was detected

Technical difficulties have been few and wholly concerned with the catheter   It has blocked on three occasions   One catheter was so flexible that control of the tip was not found possible   The outer plastic covering of another, apparently sound on introduction split completely round its circumference within the lumen of the peripheral vein, during intracardiac manipulation of the tip by rota-

tion of the butt externally   Angled terminal openings in a set of catheters made withdrawal of blood from any venous radicle capricious   Specially ground adaptors have had to be made for some catheters to ensure an air-tight junction between the catheter and the syringe

With suitable catheters and average skill, no technical difficulty need be anticipated in performing cardiac catheterization   An occasional failure is to be expected from a persistently abnormal catheter course   The danger of precipitation of a cardiac arrhythmia is real

CARDIAC INFARCTION WITH PAIN CONFINED TO EFFORT

BY A MORGAN JONES AND E J WADE

The authors have reviewed 98 consecutive cases of angina of effort   Eight have died or can not be traced, 90 have been re-interviewed to ascertain whether there has ever been any clinical episode suggestive of infarction   In 62 cases the pain was typical in every respect of angina of effort, being confined to exertion, invariably relieved by rest, and never lasting more than 15 minutes   Unless there was unequivocal evidence of infarction in the routine electrocardiograms, a full electrocardiographic investigation was made, including standard leads, unipolar limb leads, 6 unipolar præcordial leads, and 6 high unipolar præcordial leads   Infarction was diagnosed when two of the following changes were present in leads facing ventricular muscle (1) typical QRS changes, (2) S–T changes, (3) T wave changes not explicable by ventricular enlargement   T wave changes alone were not accepted as proof of infarction

In the 62 selected cases typical changes of cardiac infarction were present in 17 (28 per cent), and abnormal electrocardiograms suggestive of infarction were found in 12 (19 per cent)   Abnormal cardiograms, not suggestive of infarction, were present in 5 cases (8 per cent), and in 28 cases (45 per cent) the cardiogram was within normal limits

CORONARY ATTACKS IN GENERAL PRACTICE

BY C PAPP

Coronary attack is a clinical term for persistent anginal pain, lasting half an hour or more, arising at rest and unresponsive to trinitrin

Twenty seven patients seen in general practice and treated for coronary attacks were investigated, according to the gravity of the clinical symptoms and blood sedimentation rate (B S R), they were divided into three groups, of slight, moderate,

and severe coronary attacks   Electrocardiography was used for diagnosis but disregarded for assessment   It confirmed recent myocardial ischæmia in 20, and was inconclusive in 5, no records were obtained in 2 patients who died early

Slight coronary attack   12 cases, no death, 7 confirmed, 5 unconfirmed by electrocardiogram, this latter group includes 4 with severe hypertension (3 women) and one with Buerger's disease   Pain was moderate, and relieved by single injection of morphia gr ¼–½ and rarely recurred   The fall of blood pressure was short-lived and slight   Pyrexia was present only in a few   The B S R. was either normal from the onset or went back to normal within a fortnight   Shock and pulmonary congestion were absent and so were cardiac signs except for occasional ectopic rhythm during the attack

Moderate coronary attack   5 cases, none fatal, and all confirmed by electrocardiogram   Pain was severe, and repeated injections of morphia were often required (total amount gr ½–¾)   Pain often recurred in a slighter form after the attack   Shock was slight or moderate, always relieved by morphia and never lasting longer than the pain   Blood pressure might fall considerably and return to normal only after a fortnight or more   Pyrexia was present for a few days   B S R was back to normal at the end of three to four weeks   Cardiac and pulmonary signs were absent

Severe coronary attack   10 cases, of these 7 died   Pain was often in three phases   The main attack was preceded by a slight coronary attack, often in the form of short and repeated attacks of angina at rest, responding to trinitrin   Rest in bed did not prevent the second phase, the main attack, which was characterized by extreme pain or by pain of 24 to 48 hours' duration   This was relieved by intravenous and subcutaneous morphia (total amount gr ¾–1 with added atropine)   The third phase, consisting of further attacks requiring morphia, often followed and was fatal in 3   Shock, severe and protracted (fatal in 4), was the leading symptom in this group, it produced fall of blood pressure to dangerous levels and permanent lowering in those who recovered, it was also responsible for pulmonary congestion and the high incidence of heart failure (5 cases)   Pyrexia was high after shock had subsided   The return to normal of the B S R was delayed by pulmonary complications   Cardiac signs such as persistently high pulse rate, triple rhythm, and apical systolic murmurs were precursors of congestive heart failure   Death was due to shock (4 cases), congestive heart failure (1 case), pulmonary embolus (1 case probable) and to coronary attack during sleep (1 case probable)   Death

from shock occurred within hours, from congestive heart failure within months, or from further coronary attack at any time, the last could not be foretold by the electrocardiograph

Electrocardiographic signs were in broad agreement with clinical signs   In slight and moderate coronary attacks temporary or definite inversion of T in one or more leads was found   In severe coronary attacks, current of injury, Q waves, and later deep inversion of T were the prominent features   In a few discordant cases, clinical signs proved of greater prognostic value than the electrocardiogram

Treatment was adapted to gravity   Slight and moderate coronary attacks required symptomatic treatment only   Rest in bed was reduced to two weeks in the slight and to three or four weeks in the moderate group, according to the return to normal of the B S R   Angina of effort was not provoked by the shorter rest and could not be prevented by extension of rest   The prognosis in slight and moderate coronary attack was favourable, and 16 out of 17 patients were active in profession, business, or household   In severe coronary attacks shock needed active treatment, oxygen tent might be life-saving and anti-coagulant treatment was a necessity, particularly if pulmonary complications were present   Dicoumarol was not used because of its dangers, heparin was safe without laboratory control   Intravenous theophylline-ethylene-diamine combined with ouabaine or oral digitalis was used at the first signs of failure   Recovery from a severe coronary attack was uncommon over the age of 60, those who survived in this series were of the younger age group, and only one of the three recovered without residual cardiac damage

THE RADIOLOGY OF HEART FAILURE DUE TO CARDIAC INFARCTION

BY FREDERICK JACKSON (*introduced*)

Teleradiograms were taken before and after treatment in 8 cases of heart failure following cardiac infarction without hypertension   In 4 the heart was only slightly enlarged during failure   In the other 4 it was moderately enlarged, but returned almost to normal size with treatment in 2, hydropericardium was suspected in these and confirmed once at necropsy   The enlargement persisted in the other 2 cases

The special features of this variety of failure are these   It may occur in a heart that is almost normal in size   During failure the heart usually enlarges, but not greatly, and it may scarcely enlarge at all   With treatment the heart may return very nearly to normal size   The enlargement may be due

to hydropericardium, as was shown once post mortem   Raising of the diaphragm, pulmonary congestion, and hydrothorax are usual   They may develop or largely disappear in as short a time as one week, but generally take longer

NON-RHEUMATIC INTERSTITIAL MYOCARDITIS

BY FLORENCE MCKEOWN (*introduced*)

The incidence of interstitial myocarditis has been investigated in routine post-mortem material   It was found to be present in 2 per cent of cases   There was a tendency for it to occur in association with certain infections with some frequency, and it has been observed in pneumonia, meningococcal septicaemia, diphtheria, and miliary tuberculosis

The author discussed its relative importance in these conditions   A further group of isolated myocarditis was included, in which it was impossible to establish a correlation with any existing infection

SOME CHARACTERISTICS OF INSTRUMENTS DESIGNED FOR RECORDING ELECTROCARDIOGRAMS AND HEART SOUNDS

BY A MORGAN JONES AND M G SAUNDERS (*introduced*)

The determination and importance of the range of frequency response and of the duration of the time constant in electrocardiographs and cardiophonographs were discussed and illustrated by the characteristics of certain commercial recorders

THE PHONOCARDIOGRAM OF AORTIC STENOSIS

BY A LEATHAM

Aortic stenosis produces a murmur of characteristic shape in the phonocardiogram both in the aortic and in the mitral areas   It often starts late in relation to the electrocardiogram and finishes well before the second sound, but sounds have high-frequency components simulating murmurs and it may be difficult to tell where one ceases and the other begins   In each of 20 subjects with aortic stenosis but without evidence of mitral valvular disease, the systolic murmur was small at its onset and rose to a peak in mid systole, then diminished in size until it was small or absent at the second sound   Though the mid-systolic accentuation was greatest in the aortic area it was always present in the mitral area   In most cases the second sound was followed by an early diastolic murmur

In mitral valvular disease the systolic murmur was earlier and reached the second sound, there was no sharp mid systolic accentuation

In a group of some 20 cases of pulmonary stenosis there was also a mid-systolic accentuation, but it was seldom so great as in aortic stenosis and the murmur usually reached the second sound

The phonocardiogram of aortic stenosis may prove of value in clinical diagnosis when the systolic murmur is loud at the apex   The shape described was found in all cases of aortic stenosis so far examined and was different from the shape in mitral valvular disease   Whether it is truly distinctive or whether it may be simulated in some other condition remains to be determined

EXAMINATION OF THE HEART AT NECROPSY

BY J SHILLINGFORD (*introduced*)

A closer examination of the heart at necropsy than the one usually carried out has been developed at the London Hospital during the past year

The coronary arteries are injected with a radio-opaque substance, and an apparatus has been designed to facilitate this technique as a routine method of examination   The correlation between filling defects as shown on the X-ray and arterial lesions has been studied

Cardiac chamber volume has been measured by means of wax casts, and a simple method of making these has been found   Hypertrophy of the muscle wall is shown by multiple measurements and a standard for normals has been established

For the most part, the examination has been developed to correlate autopsy findings with those in life as shown by the multiple chest lead electrocardiogram

ABSTRACTS OF CARDIOLOGY

Asymptomatic Heart Disease Observations Made during the Early Recruiting Period for Navy and Marine Enlistments. A S HYMAN *Amer J Med 5*, 351–364, Sept , 1948

Of 1900 boys and men examined before enlistment in the Navy or Marine Corps and referred to a cardio-vascular specialist 350 were found to be suffering from some form of asymptomatic cardiovascular disease, as regards which the history was entirely negative The ages varied between 17 and 51, average 26, the smallest age groups were those of 47, 49, 50, and 51 years with 3 cases each Valvular heart disease was found in 169 (mitral insufficiency 93, mitral stenosis 41, aortic in competence 22, aortic stenosis 9, congenital lesions 4), and hypertension in 89 (systolic pressure 150 to 170 mm Hg., 58, 170 to 190 mm , 25 190 to 210 mm , 5, 210 to 220 mm 1) It is emphasized that high blood pressure may develop without giving rise to any symptoms and that pathological signs start to develop with pressures exceeding 170 mm Hg Arrhythmias were present in 55 (ventricular extrasystoles 18 auricular 6, nodal 2, and bifocal 1, tachycardia of or exceeding 110, 19, auricular fibrillation 6, complete heart block 2, and incomplete heart block 1) Cardiac hypertrophy was found in 26, of whom 22 had engaged in athletics (15 in more than moderate degree) This was the most common single factor found in this group Premature arterial changes were found in 11 Only those in the group with premature contractions and 4 amongst the 26 with cardiac hypertrophy were accepted for service The explanation for the absence of symptoms in these conditions in the examined group is discussed

A Schott

Arterial Blood Pressure in Labour and the Puerperium D Y DARON *Akush Ginek* , No 5, 10–13, 1948

The variations in the blood pressure during normal labour were studied in 45 women Systolic pressure in 37 at the beginning of labour was between 105 and 125 mm Hg , varying in the remainder from 130 to 155 mm During the first stage systolic pressure tended to be higher in primiparæ and younger women During the second stage, contrary to expectation, systolic pressure changed little, save in rapid labours In most cases the systolic pressure rose in the third stage (in 30 by 15 mm , in 7 by 20 to 40 mm), this rise was most marked in rapid labours and in younger women After placental expulsion, systolic pressure returned in 36 forthwith to normal, return being slower after longer labours

Diastolic pressure in 35 women exceeded 70 mm Hg at the onset of labour During the second stage in most cases it either rose by 10 to 20 mm or remained unchanged During the third stage it rose still further,

only to fall again in most cases after expulsion of the placenta Diastolic pressure was highest in older women and in more rapid labours When labour was prolonged there was usually a sharp rise soon after expulsion of the fœtus

Changes in the character of the pulse are described The work of the heart was also studied by the use of Lilienstrand coefficient The cardiovascular system was not subjected to undue stress in either the first or the second stage, the greatest burden being placed on it after expulsion of the fœtus by the sudden alteration in intra abdominal pressure

S S B Gilder

An Analysis of Certain Factors Associated with the Production of Experimental Dissection of the Aortic Media, in Relation to the Pathogenesis of Dissecting Aneurysm J S ROBERTSON and K V SMITH *J Path Bact* 60, 43–49, Jan , 1948

The pressure required to produce experimental dis section of the aorta by forcing water through a needle into the media was measured in 42 adults of different ages and both sexes In all cases this pressure was far higher than the blood pressure even in severe hypertension These results (which were well analysed statistically) support the view that aortic dissection only occurs in cases of marked medial degeneration

D M Pryce

Thrombosis as a Factor in the Pathogenesis of Aortic Atherosclerosis J B DUGUID *J Path Bact* 60 57–61, Jan , 1948

Recent thrombotic deposits were found in the aorta in 19 of 50 cases post mortem Whilst most frequent over atheromatous ulcers of older subjects they were also found in association with early atheromatous streaks and even where the wall appeared normal Often the deposits were superimposed on earlier deposits Transitional appearances indicated that the deposits were gradually transformed into intimal thickenings which would ordinarily have been regarded as purely arteriosclerotic The author has previously shown the importance of this process in the coronary arteries *D M Price*

The Application of Oximetry and Cardiac Catheterization to the Diagnosis of Congenital Heart Disease H B BURCHELL *J Iowa med Soc* , 38 364–368 Aug 1948

The diagnosis of congenital heart disease by the traditional methods is notoriously difficult Apart from those cases with such typical features as the murmurs of a patent ductus arteriosus and the tremendous pulsa

tions of the hilar vessels in atrial septal defect, so-called pathognomonic signs are rare   The author describes the use of the cardiac catheter together with a photo-electric oximeter in the investigation of these cases   The oximeter permits recognition of degrees of unsatura-tion of arterial blood with oxygen which are insufficient to cause recognizable cyanosis   In Fallot s tetralogy the degree of pulmonary stenosis may be estimated by the extent of the fall in arterial oxygen saturation during exercise   In the most severe cases this may fall as low as 20%   Those patients who cannot maintain an arterial saturation of at least 70% at complete rest are in a very precarious condition

Catheterization of the heart involves accurate radio-logical studies of   (1) the position of the catheter tip together with observations on (2) intracardiac pressure, and (3) variations in oxygen saturation of the blood in the various positions   Without all these it is impossible to decide the exact location of the catheter tip within the heart owing to the great deviations from normal pressures which may take place in the presence of complex con-genital defects   The oximeter may be used for rapid determination of oxygen saturation of any sample of blood withdrawn through the catheter   Pressures within the heart are recorded with sufficient accuracy for clinical purposes by means of strain-gauge manometers

The recognition of an atrial septal defect is one of the easiest examples of the use of this method   Its presence may be determined by the ease of passage of the catheter through the defect into the left auricle or pulmonary veins and also by the finding of arterialized blood in the right atrium   Similarly, arterialization of blood in the pulmonary artery is practically diagnostic of patent ductus arteriosus   High right intraventricular pressures with normal pulmonary artery pressures are always suggestive of pulmonary stenosis   The author points out that the calculations used by Bing for the assessment of pulmonary blood flow and other factors need further critical re-evaluation on account of various inaccuracies which may arise in the techniques used   He also points out that the clinical features of the various congenital lesions often permit of diagnosis with fair certainty, and cardiac catheterization is of most value in atypical cases   Angiocardiography is also of immense value in the study of such problem cases   *J McMichael*

Hoarseness in Heart Disease   J L THOMPSON and A D KISTIN   *Ann intern Med*   29 259–273, Aug., 1948

The authors were able to find only 30 reported cases of left recurrent laryngeal nerve palsy associated with heart disease in which necropsy findings were recorded   Dilatation of the pulmonary artery was the prime cause of the nerve injury   They describe 2 cases of their own in which the sole initial complaint was hoarseness

The literature is reviewed at some length and the various explanations of the etiology are given   It had been suggested that the combination of heart disease and recurrent laryngeal paralysis is so infrequent that their association is purely coincidental   many cases remain unexplained   In mitral stenosis paralysis of the nerve

has been found ten times as often as in hospital patients in general, and, were the association coincidental, the right and the left nerve ought to be equally affected   No case is recorded of paralysis of the right nerve alone and where both nerves were held to be affected there has been no necropsy   Attempts have been made to link the paralysis with the presence of the ligamentum arteriosum as it passes backwards from the left pul-monary artery to the aorta, but the evidence is con-tradictory   In most of the cases studied pulmonary artery dilatation was a common factor, but the fact remains that   while such dilatation is frequent, associated laryngeal nerve paralysis is rare

Case I is illustrated by a skiagram of the right oblique view with barium filled œsophagus, photomicrographs, and photographs of the dissection   In these photo-graphs the anatomical relations of the various parts are seen with clarity   In Case II the angiocardiograms are reproduced with explanatory diagrams   *Donald Hall*

The Effect of Exercise on the Electrocardiogram [Master " Two-step " Test] in the Diagnosis of Coronary Insufficiency   D UNTERMAN and A C DeGRAFF   *Amer J med Sci*, 215, 671–685, June, 1948

A standard two-step exercise test (Master *Amer J med Sci* 1929, 177, 223) was used and electrocardiograms (leads I, II, III, and CF4) were taken as quickly as possible afterwards   The criteria for a positive test, which were adopted as more marked than the changes seen in 31 normal controls, were as follows   (1) A depression of the RS–T junction of more than 1 mm in the standard leads or more than 0 75 mm in CF4 this lead being standard-ized at half the usual sensitivity   (2) Conversion of an upright T wave to an isoelectric or inverted T wave in leads I, II, or CF4 or of a diphasic or inverted T to upright

The test was tried in 91 patients with various forms of heart disease, with positive results in 31   Positive results were obtained in 48% of patients with typical angina, 24% of those with atypical symptoms and in 28% of those without pain   Ten patients experienced anginal pain during the exercise and in 7 of these the test was positive   The influence of food, digitalis, and recent acute illness is also considered

[The control group in this series consisted of younger patients than those with heart disease   The patients with heart disease are classified on an ætiological basis only, so that the possible influence of cardiac enlargement or failure cannot be determined]   *J W Litchfield*

The Immediate Sequelae of Myocardial Infarction Their Relation to the Prognosis   A SELZER   *Amer J med Sci*, 216, 172–178 Aug. 1948

A study of 130 cases of recent myocardial infarction coming to necropsy was made in an effort to determine the immediate cause of death   In 35 the patient was previously so ill that the myocardial infarction might be regarded as a terminal event   In the other 95 there was little limitation of activities before the infarction   These

patients were divisible into four groups In the first, consisting of 28 patients, death was due to progressive circulatory failure, with or without shock The 24 patients in the second group died suddenly 24 hours or more after the infarction and presumably from a fatal arrhythmia. In the third group were 32 patients who died as the result of some complication demonstrable at necropsy—rupture of the ventricle (8), embolic phenomena (15), the other complications were not directly connected with the infarction The remaining 11 patients died of miscellaneous causes—recurrent coronary occlusion (5), prolonged illness for which no cause could be found (4), and possibly digitalis poisoning (2) No correlation was found between 'the age of the patient, the severity of coronary arteriosclerosis, the size of the infarct, the presence of old scars or cardiac hypertrophy, the course and duration of the illness or the frequency of complications Thus, a considerable number of patients with myocardial infarction die, not from cardiac insufficiency, but from serious arrhythmias, thrombo-embolic phenomena, and shock   *C Bruce Perry*

Electrocardiographic Changes in Diphtheria S S ALTSHULER, K M HOFFMAN and P J FITZGERALD *Ann intern. Med*, 29, 294–305, Aug , 1948

This is a study of 600 patients in the American Occupied Zone of Germany between September, 1945, and December, 1946 All the cases reported were confirmed bacteriologically 26 being examples of cutaneous diphtheria The average age of the patients was 23 years and 37 were females An electrocardiogram was taken as soon as diphtheria was suspected clinically or a positive culture obtained, thereafter weekly or more often if thought necessary Those with severe or prolonged cardiographic changes were invariably returned to the U S A for convalescence The period of observation for patients with cardiographic changes varied between 8 and 23 weeks

Of the 600 patients 143 (24%) presented cardiographic changes at some time during their stay in hospital By far the most common abnormality was low voltage or negativity of the T wave in two or more leads (108 cases), next in frequency, but far behind, was prolongation of the P–R interval (11 cases) and depression of ST segments in two or more leads (10 cases) All cardiograms were checked independently and no borderline curves were included Of the T wave changes 30 involved leads II and III, 28 all four leads, and 25 leads I, II, and III Slight slurring and splintering of the QRS segment were common, but significant prolongation was seen only in the 2 patients with right bundle branch block Low voltage of QRS in all leads was present in 3 patients only Electrocardiographic changes were met with for the first time after the fourth week only in 5 of the 600 patients examined [The authors state that patients with persistent abnormalities in all leads usually had manifested clinically severe infections but in the summary severity of clinical infection and severity and duration of electrocardiographic changes in diphtheria cannot be correlated] It is pointed out that this study does not

support the view that prolongation of the P–R interval is the most common abnormality in diphtheria.

The two patients with heart block had been treated for haemolytic streptococcal sore throat and discharged completely asymptomatic, to duty within the week One was readmitted in 6 days the other in 8 both in cardiovascular collapse In the 2 fatal cases T waves were negative in all leads In 4 patients phasic alternation between normal and abnormal electrocardiograms was found

The paper is well illustrated by serial cardiograms and the authors consider that in diphtheria alike in the acute stage and in convalescence the electrocardiogram is essential to the evaluation of the physical state of the patient   *Donald Hall*

Dicumarol in Experimental Myocardial Infarction G V LeRoy and L A NALEFSKI *J Lab clin Med*, 33, 961–971, Aug , 1948

At first dicoumarol was used only for patients who had already experienced thrombo-embolic complications of cardiac infarction—either repeated episodes of multiple thrombosis in different areas of the coronary tree or repeated phenomena elsewhere, for example, in the lungs Later it was given purely prophylactically against such complications

The incidence of thrombo-embolic complications in recent myocardial infarction is difficult to determine as the data are conflicting the figures given by different authors vary from 9 9 to 45% Even the incidence of mural thrombosis of the endocardium is difficult to ascertain, being stated variously as between 17 and 83% However, it is evident that thrombo-embolism is an important complication of myocardial infarction The authors state that in all the reports of results of anti coagulant therapy there has been an apparently significant reduction in the number of thrombo-embolic complications and in the general mortality rate, but they point out that there has been as yet no report which includes suitable controls

The chief hazard with anticoagulant therapy is the development of a haemorrhagic state and it is essential that treatment be controlled by prothrombin determinations As the early stage of infarction is characterized by hyperaemia and haemorrhage the authors thought it possible that the use of anticoagulants might accentuate the haemorrhagic stage and thus prolong resolution of the infarct Myocardial infarction was produced in 25 dogs by ligation of the anterior descending branch of the left coronary artery Fifteen were given dicoumarol in amounts similar to those used in the treatment of patients with recent infarction The animals were killed at intervals of 5 to 22 days There were slight differences between the control group and the dicoumarol treated group but the authors state that there was no evidence that the altered coagulability of the blood affected the extent or healing of infarcts Serial electrocardiograms showed no significant difference between treated animals and controls No deleterious influence on healing was demonstrated   *S Oram*

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